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TROPICAL DISEASES BULLETIN.

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THE PHYSIOLOGY OF THE SMALL INTESTINE: ITS APPLICATION TO THE AETIOLOGY OF SPRUE.

A CRITICAL REVIEW.

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Surprisingly little is known about essential pathological changes in the small intestine which are vital to the production of intestinal disease.

In recent years the leading signs and symptoms of pernicious anaemia, sprue and pellagra have been contrasted with the object of defining some common factor linking these apparently dissimilar diseases together[1, 12, 48a].

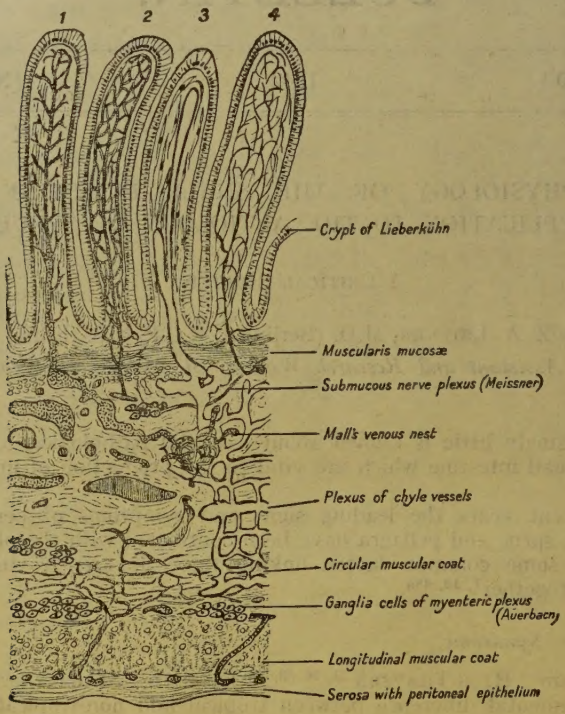
The Sprue Syndrome.

Many since HESS-THAYSEN [71, 26, 53, 30b] have stressed that there exists no fundamental difference between tropical and non-tropical sprue. Some have even suggested that the sprue syndrome is evolved from delayed coeliac disease in infancy[8]. The main points are glossitis, steatorrhoea, emaciation, progressive anaemia (usually macrocytic), hypochlorhydria—sometimes achylia with loss of intrinsic factor, hypocalcaemia, a general avitaminosis, and, it may be, pigmentation of exposed parts. The geographical distribution of tropical sprue is well known, but the number of cases of non-tropical sprue so far described is not large enough to permit of any generalization on this aspect of the subject. The *clinical picture* of tropical and non-tropical sprue can be reproduced by totally dissimilar states, such as lacteal obstruction due to tuberculosis,[63] malignant disease of mesenteric glands[20b, 48a] or gastrocolic fistula[20a, 52, 8].

So far, apart from minor anatomical changes such as aplasia, degeneration and increase of reticulum in the villi, no *destructive lesions* have been found in tropical, non-tropical sprue and in idiopathic steatorrhoea. In order to explain this anomaly a critical review of modern ideas of the physiology of the small intestine has been undertaken.

Anatomy of the small intestine as bearing on the present problem.

Apart from the well-known points of the structure of the small intestine, the mucosa consists of muscularis mucosae, tunica propria and epithelium. According to modern histological research the muscularis mucosae has an outer longitudinal and an inner circular



1. Villus with venous plexus.
2. ,, ,, arterial ,,
3. ,, ,, chyle vessel.
4. ,, ,, nerve plexus.

Section of ileum to show structure of villi. (Partly after J. SCHAFFER, "Vorlesungen über Histologie," 1924; modified by VERZÁR and McDOUGALL, 1936.)

layer extending upwards into the valvulae conniventes (Kekring) with offshoots into the villi. Meissner's plexus is mainly concerned with the innervation of the villi and is also closely connected with the muscularis. The tunica propria contains loose connective tissue, blood and lymph vessels and nerve fibres and its function is to secure proper nutrition and free movement of the epithelium, consisting as it does of a single layer of columnar cells.

The main interest in the present exposition centres on the villi: these are elevations 1 mm. by 0·1–0·25 mm. in width in number of 10 to each sq. mm. of mucosal surface. The centre of each villus is a lacteal ending blindly and accompanied by a network of nerve fibres and vessels. The

surface cells are mainly of the columnar absorbing type, but there are also mucus-secreting goblet cells, Paneth and enterochrome cells whose function is as yet unknown. In between the villi are Lieberkühn's follicles lined mainly with Paneth cells.

For the proper understanding of its functions the motility of the small intestine is important. Three types have been described :—segmenting, peristaltic and pendular. The nature of the pendular movements is not quite clear as they are only seen in the opened abdomen as to and fro movements of the intestinal contents in the same loop, and are due, apparently, to intermittent contractions of different portions of each individual loop. From the physiological aspect segmenting movements are most important. These are fairly regular and diminish in frequency with *increased* distance from the stomach : in the ileum, for instance, they occur at the rate of about twelve per minute. The term " metabolic gradient " (ALVAREZ, 1940) is used in this connexion, and indicates that the upper portions have a higher rate of metabolism and excitability than the lower. These contractions ensure a thorough mingling of the digestive fluids with the intestinal contents, and intimate contact with the intestinal wall, without any measurable translatory effect on the food column, but the progress of the chyme is caused by peristaltic waves and is effected by spiral rotation.

The bulk of the chyme, moreover, exerts a direct irritating effect on the wall, producing contraction proximal and relaxation distal to point of contact. The segmenting movements are rendered ineffective by application of nicotine or cocaine, which act on Auerbach's plexus and so abolish peristalsis[6].

Antiperistaltic movements have not been observed in the lower part of the small intestine, but if a portion is excised and reinserted in the opposite direction, partial obstruction occurs, as peristaltic waves cannot travel downwards, and in consequence the intestine above this level dilates. When, however, Auerbach's plexus is inhibited, or paralysed, this effect is abolished and food may travel upwards or downwards.

The *duodenum* is the only portion of the small intestine where antiperistalsis—usually in the second, less frequently in the third part—normally occurs, a fact which determines the periodical filling of the duodenal cap in X-ray diagnoses of duodenal ulceration.

The *biology* of the villi is a most striking feature of modern experimental physiology. The central lacteal, which has a blind end, communicates by its free end with the lymphatic plexus in the submucosa and there are valves present along its course to prevent reflux from the deeper plexus whilst safeguarding the normal flow. Contraction of the fibres of the muscularis shortens the villi and at the same time empties the central lacteal (as has been shown by microcinematographic films by KOKAS and LUDÁNY, 1930), so that as soon as absorption commences, the villi are in continuous movement, contractions occurring 3–6 times, or even more, per minute.

VERZÁR (1931) has calculated that the amount pumped out, by one contraction only, from a surface 200 cm. by 5 cm., is as much as 5 cc., which would correspond to a discharge of fluid of 15–30 cc. per minute. What then is the natural stimulus which sets this mechanism in motion ? It has been shown that mechanical stimuli applied to the base of the villus cause contraction, but that acetylcholine (which is the specific stimulus for Auerbach's plexus) has no effect. Contraction, however, is secured by amino-acids, yeast extracts, but not by pure vitamin B_1 or B_2 (VERZÁR 1936). When the mucosa is stripped together with part of the submucosa and Meissner's plexus, no movement of the villi can be elicited, but when Meissner's plexus is left, the movements are normal. The natural stimulus is probably provided by a hormone-villikinine (KOKAS and LUDÁNY, 1935 and 1938), which differs from secretin. This hormone, which is extracted from the intestinal mucosa by dilute hydrochloric acid, has been

shown to be present in the blood after hydrochloric acid has been placed in the duodenum (of experimental donor dog).

Absorption.

The forces of absorption are: filtration, diffusion and osmosis aided by surface activity, solubility and hydrotrophy on the one hand; by electrolytic forces and permeability on the other. The mechanism of absorption is promoted by the movements of the villi. For water and crystalloid solutions absorption proceeds with its diffusion gradient; if the concentration is higher in the intestines, it moves in the direction of the blood. This mechanism applies to the absorption of the carbohydrates, proteins and most minerals. With the subject of the present discussion the absorption of calcium and fats is specially important.

Calcium is absorbed only in water-soluble form and absorption is prevented by substances which form insoluble salts, such as phytic acid, oxalates, etc.[45]. It may be that the calcium-fatty-acid-bile-acid complex is broken down after absorption in the liver, or it may be that this breakdown occurs in the mucosa and that re-excretion of bile acids occurs solely through the liver (KLINKE, 1931).

Phosphorylation.

After being split by lipase in the small intestine the fatty acids combine with bile acids to form molecules which are water soluble and diffusible. The fatty acids liberated by the complex combine with glycerol to be later synthesized into neutral fat. VERZÁR (1936) has suggested that an intermediary state—phosphorylation (glycerol plus inorganic phosphate)—occurs, which accelerates absorption of carbohydrates as well as of fats by lowering concentration in the cells and by producing a continuous high diffusion gradient between both sides of the lining cells. This resynthesis aims at accelerating fat absorption as well as at rendering fatty acids non-toxic.

Relation of the vitamin B group to gastro-intestinal function.

The literature of this problem has recently been reviewed by Ross GOLDEN (1941) and there are numerous radiological studies on this subject. In a group living mainly on high carbohydrate diet irregular "deficiency pattern" of the small intestine was found (disappearance of herring-bone structure, with abnormal segmentation, coarsening and obliteration of mucosal folds), but after treatment by fractions of vitamin B all cases improved. VERZÁR and his collaborators[73, 73c] demonstrated the influence of yeast powder on contractions of the villi, but found that almost complete cessation of fat and sugar absorption takes place after adrenalectomy, or poisoning with mono-iodacetic acid; absorption is restored if cortin is supplied.

The relation of vitamin B to the adrenal cortex is very suggestive in relation to the present study. Young adrenalectomized animals do not grow if riboflavin alone is added to their food, but remain alive if flavinphosphoric acid, yeast or liver extract is added. This suggests that these substances may provide a substitute for the secretion of the adrenal cortex. *Phosphorylation is therefore one of the systemic reactions of the body responsible for the utilization of important building materials and for correlating the general bodily reactions essential for colloidal equilibrium.*

The yellow oxidizing enzymes, consisting of phosphorylated *riboflavin* plus protein (WARBURG and CHRISTIAN, 1933, 1938) constitute a most potent oxidation-reduction system. Probably the yellow enzyme represents a breakdown product of the substance in the cell with a colourless protein—probably alloxazine-adenine-dinucleotide. The action is reversible oxidation-reduction. The yellow respiratory enzymes act, usually, as part of a combined enzyme system, the activator consists of a protein plus the co-enzyme or co-zymase. This latter is a compound consisting of nicotinic acid amide plus pentose, and adenine plus pentose, both combined by a molecule of pyrophosphoric acid, di- or tri-phosphopyridine nucleotide, *i.e.* coenzyme I and coenzyme II respectively (EULER and SCHLENK, 1937). This enzyme system can act in the cells also in the absence of available iron compounds and in the presence of cyanides, sulphides and carbon monoxide, but other oxidation-reduction enzymes —the cytochromes—cannot do so under similar circumstances. (KEILIN, 1929; KEILIN and HARTREE, 1939). The essential influence of the vitamin B group on phosphorylation now appears strengthened by the recognition that the yellow enzymes are, in fact, phosphorylated combinations of riboflavin, the co-enzymes phosphorylated combinations of nicotinic acid and the cocarboxylases phosphorylated thiamin. The importance of the vitamin B group is mainly in the maintenance of phosphorylation in *intracellular* metabolism by securing a high gradient between the different colloidal systems and by warranting diffusion. Evidence in this respect has been derived from a different angle. Thus LOEB (1932) found in Addison's disease that depletion of sodium is followed by a series of interferences especially in carbohydrate and to a lesser extent in fat metabolism, so that not only phosphorylation but also permeability and osmosis are disturbed by imbalance of the electrolyte system, especially that of sodium, which is the main kation of the *extracellular*, and that of potassium, the main kation of the *intracellular* system. This may then be justly regarded as the essential disturbance in Addison's disease.

Thus, it is possible for the vitamin B group to regulate general body reactions by phosphorylation and possibly influence the cortical hormone (or hormones) by keeping up the electrolyte balance[73a]. In connexion with the cytochromes already mentioned, which are active only in presence of available iron, there are certain pathological conditions where iron-free haemoglobin derivatives (porphyrins) are increased in the circulation, in faeces and urine. In these conditions the cytochromes are put out of action, so that the main task of oxidation and reduction in cellular metabolism is taken up by the yellow enzyme-co-zymase system which contains B group vitamins. In some such manner as this a deficiency of these vitamins is bound to ensue.

The relation of porphyria to intestinal dysfunction.

Porphyrin appears to be a normal breakdown product of haemoglobin and out of the various varieties of the former pigment uroporphyrin is exclusively excreted in congenital porphyria*[13, 17, 62]. Porphyrins, when broken down, are absorbed by the intestines, and are re-excreted with the bile in a manner similar to that of bilirubin.

* The term porphyria is reserved for the syndrome. Porphyrinuria simply indicates abnormal excretion of porphyrin in the urine without characteristic symptoms and signs.

Porphyria is mainly of interest because of its relation to abdominal abnormalities caused by the action of this pigment on the autonomic nervous system of the intestine. When injected intravenously, or applied locally, it interrupts the normal rhythmic contractions of the intestine (REITLINGER and KLEE, 1928), and application of atropine does not restore the normal intestinal automatism (VANNOTTI, 1935). Prostigmine, on the other hand, produces movements in the porphyrinized small intestine. Facts accumulated show that the local nervous mechanism of the intestine (Meissner's plexus) is inhibited by porphyrins, and as this plexus is vitally connected with the motility of the villi, increased porphyrin leads to inhibition of absorption[72].

This porphyrin reaction does not appear synchronously at all parts of the bowel, so that spasms with atony may occur in the same part of the intestine. When the reactions of the autonomic nervous system are paralysed, or inhibited, the clinical and X-ray picture of an acute ileus may be reproduced, and this is what actually appears to happen to an acute attack of porphyria.

These physiological data have a distinct bearing on clinical medicine as evinced by the history of the following patient, a healthy looking man of 46 with enlarged congested liver (probably alcoholic). After an attack of vomiting a barium meal showed a normal stomach (Figs. 2, 3), a diluted duodenal bulb and a partial obstruction at the junction

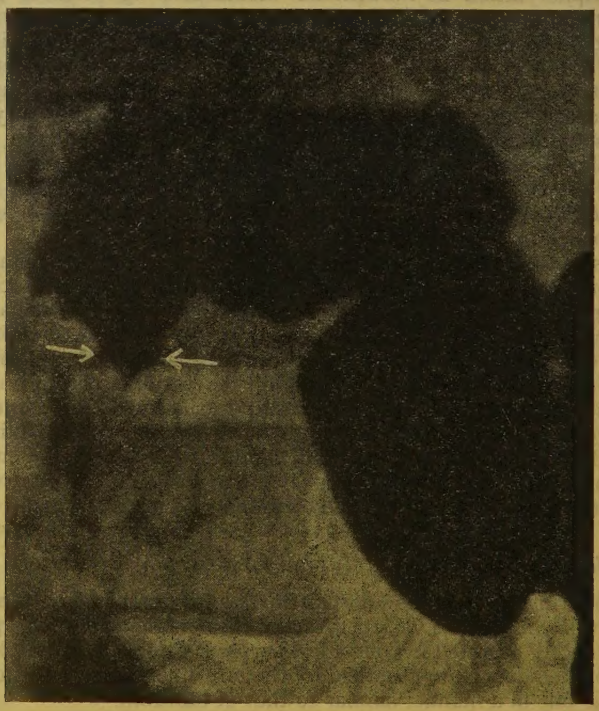


Fig. 2. Partial obstruction at the junction of the first and second parts of the duodenum with megabulbus (no anatomical lesion was found at the operation).

Fig. 3. Abnormal mucosal pattern and narrowing of the lumen of the upper jejunum. No dilatation, no changes of the mucosal pattern above the stricture. Megabulbus without dilatation of the stomach.

of the first and second portions of the duodenum. Some three months later he still appeared well, though the dyspepsia and vomiting had increased and there was some loss of weight. This time a barium meal was more positive, showing appreciable dilatation of stomach and duodenum with a six hour hold up. Immediate laparotomy showed, not, as had been suspected, an obstruction in the duodenum, but an annular stricture in the upper jejunum (adenocarcinoma without glandular metastasis) necessitating resection of 14 inches of intestine with mesentery attachment. Within a week alarming symptoms of vomiting, abdominal pains and deep toxaemia necessitated a further laparotomy, and within two months four altogether had been performed. On the second adhesions were found, on the third and fourth jejunal anastomosis and gastro-enterostomy carried out. Recovery was sure but slow and at the end of 1941 he had become stronger and had regained weight, but now there was steatorrhoea (total fat 54·8 per cent., of which 77 per cent. was split). Once again severe abdominal attacks recurred with visible abdominal peristalsis and now there was achlorhydria (without response to histamine), macrocytic anaemia, hypocalcaemia (8·6 mgm. per cent.), serum bilirubin was 1·2 mgm. per cent., blood urea 26 mgm. per cent., serum sodium 324 mgm. per cent., serum phosphatase 56·2 units in 100 ml., van den Bergh direct delayed; the laevulose tolerance test showed liver damage. Also there was porphyrinuria (742γ ether-soluble porphyrin in a 24-hours specimen of urine (normal daily excretion is 20–50γ). The stool contained 31·4γ per dry gm. weight (normal 20γ). At

this stage he was given 50 mgm. nicotinic acid, 1 mgm. riboflavin, 2 cc. crude liver extract, 5 mgm. thiamin in 10 cc. of 10 per cent. calcium-gluconate, every other day, with the result that immediate improvement took place with cessation of abdominal attacks. The urine, however, still contained increased porphyrin.

The genesis of this case is a problem for discussion. The main point in its citation lies not so much in the fact of the diagnosis of carcinoma, but in the situation of the lesion and the biochemical changes thereby produced. It may well be an example of post-operative jejuno-ileal insufficiency (BENNETT & HARDWICK), or post-operative symptomatic sprue. It nevertheless clearly demonstrated that the changing over from a pancreatic to "sprue-like" steatorrhoea is closely related to increased porphyrin production and excretion; and it gives point to the intimate interconnexion of grave intestinal disturbance and steatorrhoea, which have already been set forth on biochemical grounds. Three similar cases [49, 72b] have been found in the literature.

DISCUSSION.

(An attempt to correlate the complex physiological changes with the conception of the functional pathology of sprue.)

The primary cause, which may eventually lead to complete dysfunction of the small intestine, may not necessarily be very serious. It is well-known from routine X-ray examinations that in acute, as well as in subacute, enteritis the motility of the small intestine, especially that of the jejunum, may be increased for days. Recovery may be complete because the small intestine has an ample range of compensatory mechanism at its disposal, but on the other hand, it may increasingly affect the whole mechanism of absorption, so that split fat in excess is always present in the stools in quiescent periods without diarrhoea. The development of the full sprue syndrome probably depends on the coexistence of a number of dyskinesias and dysfunctions which may not affect the individual seriously for a long time. The aetiology of the sprue syndrome has been reviewed critically by MANSON-BAHR (1941) who considers that gastro-duodenal insufficiency is responsible for pernicious anaemia, jejuno-ileal insufficiency is responsible for the sprue syndrome and ileo-colic insufficiency for pellagra. He has also stated that neither achylia gastrica nor hypochlorhydria is present as an invariable rule in sprue. CASTLE *et al.* (1935) found the intrinsic factor present in sprue even in cases with complete achlorhydria. Although it appears that gastric acidity has no definite bearing on the progress of the disease, disturbances of gastric secretion are too frequent in sprue to be completely disregarded[29, 71].

For the purpose of the present hypothesis it may be permissible to stipulate that there exists an additional unknown factor in gastric secretion. It may be mentioned that in addition to *gastrin* (identical with histamine) a second gastric hormone has been prepared[39], from the acid extract of the pyloric mucosa, which exerts no effect on blood pressure, pancreatic or bile secretion, but when absorbed by the small intestine produces a gastric flow rich in acid, but poor in pepsin. The next link appears to have been provided by LAURENT and SINCLAIR (1938) who showed that vitamin B_1 might be destroyed in the stomach in achlorhydria; moreover, this might also take place in the gastric and duodenal juices, incubated *in vitro*, of patients with achlorhydria

(SINCLAIR, 1939; MELNICK, *et al.*, 1941), or conversely that the same might happen, even in *acid* juice in the presence of haemin (MAHLO, 1938; SCHRÖDER, 1939).

The normal and natural stimulus for the contraction of the villi and absorption is *villikinine* which is extractable from the intestinal mucosa by hydrochloric acid, so that it can now be stipulated with some confidence that some factor in the gastric juice, usually combined with hydrochloric acid, is jointly responsible, not only for the movements of the villi, but also for the preservation of vitamin B.

The permeability of the epithelium of the villi is also an important factor. For the water and crystalloids physiochemical laws of diffusion and osmosis suffice; in insoluble substances the principle of hydrotropy was introduced (NEUBERG, 1916). The principal agents in this respect are bile acids and their salts (VERZÁR, 1931).

The main chemical reaction for the maintenance of the gradient of absorption is *phosphorylation.* The catalysts responsible for the motility of the villi and also for diffusion, osmosis, hydrotropy and phosphorylation are the oxidation-reduction enzymes—the cytochromes, and in case they are rendered inactive by absence of available iron, the yellow respiratory-co-enzyme system, which is composed in turn of phosphorylated riboflavin and phosphorylated nicotinic acid. *It is tentatively submitted that in this evidence lies the importance of the vitamin B group in the sprue syndrome and allied states.* This process of substitution between these two catalyst systems in absence of available iron leads to a gradual depletion of the vitamin B group reserves. It may be assisted by other as yet unknown systems, and their interaction may be so perfect for a long period that therein may lie the well founded clinical observation of the slow development of sprue.

The question now arises as to what conditions may produce a lack of iron in cellular metabolism. It may be due to excessive intestinal putrefaction. In this connexion SEYDERHELM (1922), DIXON *et al* (1925) obtained improvement in pernicious anaemia by treatment with ileostomy followed by colonic irrigation, which mitigated the pathological flora of *Bact. coli.* Experimental intestinal strictures produced macrocytic anaemia if excessive bacterial growth prevailed above the strictures. HORSTER (1935) found that under these circumstances macrocytic anaemia, indicanuria and liver damage could be prevented by injections of liver extract or by feeding with trichlorocresol. RHOADS and MILLER (1938) found that a similar anaemia could be produced by feeding on indol and skatol, but the anaemia could be prevented by liver extracts. As an explanation it is found that certain strains of *Bact. coli* are able to de-aminize amino-acids, especially tyrosine in the small intestine; the resulting tyramine, when injected, produces macrocytic anaemia and liver damage. It is known that the liver principle (LEITNER, 1928) exerts a detoxicating effect on the liver. The acid gastric juice is responsible for checking the migration of the bacterial flora to the upper part of the small intestine, but when reduced or absent, as in sprue, intestinal putrefaction is bound to be increased. KÄMMERER (1924, 1929) has shown that intestinal bacteria are capable of producing porphyrin from haemoglobin, from myoglobin and even from chlorophyll, and that the appearance of porphyrins reduces the production of bile.

In the sprue syndrome the excretion of bile acids and salts is reduced, serum bilirubin raised and the glucose tolerance curve is flat. All

these taken together may be expression of severe liver damage so that loss of detoxicating power of the liver may be responsible for the macrocytic anaemia.

An increased porphyrinuria has been shown to exist in cases of non-tropical sprue[49, 72c] and also in the special instance quoted in this paper. It is therefore suggested that similar changes might be found in all cases of tropical sprue if investigated from this viewpoint. It is all the more suggestive as an increased porphyrin excretion in endemic pellagra has been confirmed by many workers[7, 18, 5] and similar findings have been repeatedly made in pernicious anaemia during relapse. (DOBRINER and RHOADS, 1940).

In conclusion the following views are expressed as an explanation of the chain of events involved in the mechanism of the sprue syndrome:

Primary cause.

1. Breakdown of normal absorption in the upper part of the small intestine (due to different causes).

Secondary causes.

2. Deficiency in gastric secretion and hydrochloric acid necessary for coordination of intestinal functions.
3. Achlorhydria, which affects motility of the villi and decreases the vitamin B content of food.
4. Stagnation and malabsorption, which produce abdominal discomfort and flatulence.
5. As a consequence of achlorhydria, migration and multiplication of intestinal flora (*Bact. coli*).
6. Consequent breakdown of iron metabolism in relation to bone-marrow and haemoglobin, producing megalocytic anaemia.
7. Haemoglobin metabolism perverted to increasing amounts of porphyrin.
8. Bilirubin excretion reduced; bilirubin serum content increased.
9. Following liver damage bile acids decreased; in turn reducing hydrotropy and fat absorption.
10. Unresolved fatty acids in the small intestine forming insoluble calcium salts; this affects the bones and then the whole electrolyte equilibrium. Development of this stage is slow and may last years.
11. Increasing liver dysfunction; excessive porphyrinuria whereby Meissner's plexus is paralysed; motility of villi is disturbed. Breakdown of cytochrome-enzyme system and steatorrhoea.
12. Owing to already present dysfunctions an acute vitamin B deficiency is thereby produced.

The clinical manifestations resulting from this successive chain of events may eventuate in sprue or possibly in pellagra.

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References.

1 Alessandrini, P. (1934), *Arch. Ital. mal. app. digest*, **2**, 631.
2 Alvarez, W. C. (1940). An introduction to gastro-enterology. London.
3 Barker, W. H. and Hummel, L. E. (1939), *Johns Hopk. Bull.*, **64**, 215.
4 Barnes, R. H., Wick, A. N., Miller, E. S. and MacKay, E. M. (1939), *Proc. Soc. Exp. Biol. & Med.*, **40**, 651.
5 Bassi, U. (1934), *Clin. Med. Ital.*, **65**, 241.
6 Bayliss, W. M. and Starling, E. H. (1901), *J. Physiol.*, **26**, 125.
7 Beckh, W., Ellinger, P. and Spies, T. D. (1937), *Quart. J. Med.*, **6**, 305.
8 Bennett, T. I. and Hardwick, C. (1940), *Lancet*, **2**, 381.
9 Bomford, R. R. and Rhoads, C. P. (1941), *Quart. J. Med.*, **10**, 175.
10 Bruce, H. M. and Wien, R. (1940), *J. Physiol.*, **98**, 375.
11 Capelli, F. (1936), *Med. del Lavoro*, **27**, 97.
12 Castle, W. B., Rhoads, C. P., Lawson, H. A. and Payne, G. C. (1935), *Arch. Int. Med.*, **56**, 627.
13 Chandler, F. G., Harrison, G. H. and Rimington, C. (1939), *Brit. Med. J.*, **2**, 1173.
14 Cramer, W. (1928). Fever, heat regulation, climate and the thyroid-adrenal apparatus. London.
15 —— and Ludford, R. J. (1925), *J. of Physiol.*, **60**, 342.
16 Dixon, C. F., Burns, J. G. and Giffin, H. Z. (1925), *J. Amer. Med. Assoc.*, **85**, 17.
17 Dobriner, K. and Rhoads, C. P. (1940), *Physiol. Reviews*, **20**, 416.
18 Ellinger, P. and Dojmi, L. (1935), *Chem. & Ind.*, 507.
19 Euler, H. and Schlenk, F. (1937), *Z. f. physiol. Chem.*, **246**, 64.
20 Fairley, N. H. (1930), *Trans. Roy. Soc. Trop. Med. & Hyg.*, **24**, 131.
20a —— and Kilner, T. P. (1931), *Lancet*, **2**, 1335.
20b —— and Mackie, F. P. (1937), *Brit. Med. J.*, **1**, 375.
21 Fränkel, E. (1924), *Virchows Arch.*, **248**, 125.
22 Frazer, A. C. (1940), *Physiol. Rev.*, **20**, 561.
23 Garrod, A. E. (1893), *J. of Path.*, **1**, 187.
24 Golden, Ross. (1941), *Radiology*, **36**, 262.
25 Günther, H. (1922), *Erg. allg. Path. und path. Anat.*, **20**, 607.
26 Hansen, K. (1937), *Dtsch. Med. Wschr.*, **63**, 849.
27 Harris, S. (1941), Clinical Pellagra. London.
28 Horster, H. (1935), *Z. f. ges. exp. Med.*, **95**, 514.
29 Hotz, H. W. and Rohr, K. (1938), *Erg. inn. Med.*, **54**, 174.
30 Hurst, A. F. & Knott, F. A., (1930), *Quart. J. Med.*, **24**, 171.
30a ——. (1941), *Brit. Med. J.*, **2**, 857.
30b ——. (1942), *Guy's Hosp. Rep.* (in press).
31 Jeckeln, E. (1939), *Virchows Arch.*, **303**, 393.
32 Kämmerer, H. (1924), *Dtsch. Arch. klin. Med.*, **145**, 257.
32a ——. (1929), *Verh. dtsch. Ges. inn. Med.*, Wiesbaden.
33 Keilin, D. (1929), *Proc. Roy. Soc.*, **104B**, 206.
33a —— and Hartree, E. F. (1939), *ibid.*, **127B**, 167.
34 Kendall, E. C. (1938), *Proc. Staff. Meet. Mayo Clin.*, Rochester, **13**, 379.
35 Klinke, K. (1931), Mineralstoffwechsel. Leipzig.
36 Kokas, E. and Ludány, G. (1930), *Pflügers Arch.*, **225**, 421.
37 ——. (1935), *ibid.*, **236**, 166.
38 ——. (1938), *Quart. J. Exper. Physiol.*, **28**, 15.
39 Komarow, S. A. (1938), *Amer. J. Physiol.*, **123**, 121.
40 Krebs, H. A. (1940), *Biochem. J.*, **34**, 460 and 775.
41 Laurent, L. P. E. and Sinclair, H. M. (1938), *Lancet*, **1**, 1045.
42 Leitner, Z. A. (1928), *Haematologica*, **10**, 1.
43 Lepore, M. J. and Golden, Ross. (1941), *J. Amer. Med. Assoc.*, **117**, 918.
44 Loeb, R. F. (1932), *Science*, **76**, 420.
45 McCance, R. A. and Widdowson, E. M. (1942), *J. Physiol.*, **101**, 44.
46 Mackie, F. P. and Fairley, N. H. (1934), *Trans. Roy. Soc. Trop. Med. & Hyg.*, **27**, 340.
47 Mahlo, A. (1938), *Dtsch. Med. Wschr.*, **64**, 496.
48 Manson-Bahr. (1915). A report on researches on sprue in Ceylon. Cambridge University Press.
48a ——. (1940), *Lancet*, **2**, 317.
48b ——. (1941), *Trans. Roy. Soc. Trop. Med. & Hyg.*, **34**, 347.
48c ——. (1941), *Trop. Dis. Bull.* **38**, 123.
49 Markoff, N. (1940), *Schweiz. Med. Wschr.*, **70**, 1137.
50 Martin, G. J., Thompson, M. R. and Carvajal-Forero, J. (1941), *Amer. J. Digestive Dis.*, **8**, 290.

51 MELNICK, D., ROBINSON, W. D. and FIELD, H. (1941), *J. Biol. Chem.*, **138**, 49.
52 MINDLINE, J. and ROSENHEIM, M. L. (1935), *Lancet*, **2**, 764.
53 MOGENSEN, E. (1937), *Quart. J. Med.*, **5**, 119.
54 NEUBERG, C. (1916), *Bioch. Z.*, **76**, 105.
55 NEVER, H. E. (1928), *Pflügers Arch.*, **219**, 554.
56 PETERS, R. A. (1940), *Nature*, **146**, 387.
57 PIJOAN, M. and OBERG, S. A. (1937), *Proc. Soc. Exp. Biol. & Med.*, **36**, 187.
58 POCK STEEN, P. (1937), *Geneesk. Tschr. Ndld. Indië.*, **29**, 1714.
59 RAU, L. (1940), *Lancet*, **2**, 647.
60 REITLINGER, K. and KLEE, P. (1928), *Arch. Exp. Path. Pharm.*, **127**, 277.
61 RHOADS, C. P. and MILLER, D. K. (1938), *J. Exp. Med.*, **67**, 273.
62 RIMINGTON, C. (1936), *Onderstepoort J. Vet. Sci.*, **7**, 567.
62a ——. (1939), *Proc. Roy. Soc. Med.*, **32**, 1268.
62b —— and HEMMINGS, A. W. (1939), *Bioch. J.*, **33**, 960.
63 RYLE, J. A. (1924), *Guy's Hosp. Rep.*, **74**, 1.
64 SCHRÖDER, H. (1939), *Klin. Wschr.*, **18**, 148.
65 SEYDERHELM, R. (1922), *Erg. inn. Med.*, **21**, 361.
65a ——, LEHMANN, W. and WICHELS, P. (1927), *Krankheitsforsch.*, **4**, 263.
66 SINCLAIR, H. M. (1939), *Proc. Roy. Soc. Med.*, **32**, 812.
66a ——. (1941), *Postgrad. Med. J.*, **17**, 3.
67 SNELL, A. M. and CAMP, J. D. (1934), *Arch. Int. Med.*, **53**, 615.
68 SPIES, T. D. and PAYNE, W. (1933), *J. Clin. Invest.*, **12**, 229.
69 STERN, C. G. (1939), *Cold Spring Harbor Symp.*, **7**, 312.
70 SYDENSTRICKER, V. P. (1941), *Ann. Int. Med.*, **14**, 1499.
71 THAYSEN, T. E. H. (1932), Non-tropical Sprue. London.
71a ——. (1935), *Quart. J. Med.*, **4**, 359.
72 VANNOTTI, A. (1935), *Z. exp.Med.*, **97**, 377.
72a ——. (1936), *Helvet. Med. Acta.*, **3**, 663.
72b ——. (1937), Porphyrine and Porphyrinkrankheiten. Berlin.
73 VERZÁR, F. (1931), *Erg. Physiol.*, **32**, 391.
73a ——. (1939), Die Funktion der Nebennierenrinde. Basel.
73b —— and LASZT, F. (1936), *Pflügers Arch.*, **237**, 473.
73c —— and MCDOUGALL, E. J. (1936). Absorption from the Intestine. London.
74 WALDENSTRÖM, J. (1937), *Act. Med. Scand.*, Suppl. 82.
75 WARBURG, O. and CHRISTIAN, W. (1933), *Bioch. Z.*, **257**, 492.
75a ——. (1938), *Ibid.*, **298**, 150.

SUMMARY OF RECENT ABSTRACTS.*

VII. HELMINTHIASIS.

General.

In a review of the mechanism of acquired immunity in helminthic infections TALIAFERRO (p. 110) points out that the evidence indicates that the humoral and cellular mechanisms are fundamentally identical with those which operate against other infections and against non-infective antigenic agents. The immediate factors are humoral, and cellular co-operation is secondary. Precipitins which are formed by the host against materials which pass out of the mouth, anus and excretory pore of intestinal nematodes give rise *in vivo* to visible precipitates, and are undoubtedly important in the allergic reactions of the host. They may also affect the immobilization, delay in development, stunting, prevention of food assimilation and inhibition of enzymatic activity of the parasite, though these actions have not been proved. In infections with larval tapeworms two types of

* The information from which this series of summaries has been compiled is given in the abstracts made by the Sectional Editors in the *Tropical Diseases Bulletin*, 1941, Vol. 38. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

immunity are developed, one early and the other late. Antibodies of the early type can be absorbed with freshly ground worm substance, but those of the late type cannot, and it is probable that the antigens stimulating the late type are liberated from the living parasite, but occur, if at all, in insufficient quantities in freshly ground worm material.

MAPLESTONE and BHADURI (p. 374) have studied the helminth parasites of dogs in Calcutta. Of the worms which infect man *Trichostrongylus colubriformis* was found, the first occasion on which it has been recorded in a carnivore. *Heterophyes heterophyes* and *Opisthorchis felineus* were also found, but though common in man in other parts of the world they are not common in Calcutta, since the Indians are protected from them by the fact that they rarely eat uncooked fish. The same applies to *Gnathostoma spinigerum*. By far the most important parasite of the dog in Calcutta is *Echinococcus granulosus*, the incidence of which is high in city dogs. *Taenia ovis* was not found in the dogs and its cysticercus was not identified in mutton, so that it is unlikely that this worm is a cause of human cysticercosis, a condition relatively common in British troops in India.

CHANG and LIN (p. 375) found infection with *Ascaris lumbricoides* in a high proportion of persons examined in Chengtu, and considerable hookworm infection in soldiers of the same area. *Clonorchis sinensis* was found there, for the first time, in man, though it is common in cats in this area; *Fasciolopsis buskii* and *Schistosoma japonicum* were also encountered.

GUNEWARDENE (p. 38) discusses the formation of phosgene from tetrachlorethylene; this apparently only occurs on exposure to light. He emphasizes the danger of testing for phosgene by smell; it is a dangerous lung irritant, even in small amounts.

Trematodes.

Schistosome infections.—Hitherto it has been thought that the littoral of Algeria has been free from indigenous infection with *S. haematobium*, though it is known to occur in Morocco. SABADINI and IMBERT (p. 39) now report an outbreak in Senegalese soldiers, Europeans and natives, in Saint-Aimé (Algiers). *Bulinus contortus* has been found in the irrigation canals of the district. L'ABBATE (p. 40) reports urinary schistosomiasis from northern Goggiam, Abyssinia, probably acquired from the water of Lake Tana or its affluents. VERMOOTEN (p. 376) points out that schistosomiasis is endemic near Johannesburg and in Pretoria and other places, at altitudes which have, erroneously, been regarded as free from danger. It is there apparently almost entirely an infection of the urinary system, and the author stresses the importance of a final cystoscopic examination in the assessment of cure. Surgical treatment is disappointing so long as infection is active.

KRAKOWER (p. 376) has investigated the effects of temperature, light, *p*H and solutions of salt on the cercariae of *S. mansoni*. In rainwater the normal life span is 24–48 hours, exceptionally 72; at 5°–6°C. life may be prolonged to as much as 14 days, but the cercariae are motionless; freezing is rapidly fatal. Up to 34°C. they live as long as at room temperature, but increasing warmth above this increases mortality, all being killed in 30 minutes at 45°C. Strong electric light induces activity and shortens life; presumably the cercariae become worn out. Ultraviolet light and direct sunlight are

both fatal, but the latter effect may be due to heat. The cercariae withstand *p*H variations from 4·6 to 10; further extremes are fatal. Sodium chloride in 1·5 per cent. solution is quickly fatal.

MARTINS (p. 42) prefers the name *Australorbis glabratus* for the intermediate host of *S. mansoni* in America. Synonyms are given, including the name *Planorbis guadeloupensis*.

BRUMPT (p. 41) describes the progress of infection of *Australorbis glabratus* with miracidia of *S. mansoni*, confirming the opinion expressed by LUTZ that the lesions observed in the tentacles are caused by the developing sporocysts.

SCOTT (p. 377) estimates that there are about 30,000 persons in Venezuela infected with *S. mansoni*, and states that the infection is practically coextensive with the distribution of *Australorbis glabratus*, the snail host. It occurs only where irrigation is in use, though the snails are not found exclusively in irrigation water. The infection is chiefly found in the valleys of the mountains along the northern coast; elsewhere the snail host is not common, and such foci as exist are small and local. In many of the endemic regions more than 90 per cent. of males aged over 10 are infected, while the proportion of females is slightly lower. Elimination of the infection by snail control is probably possible.

MEIRA and AMARAL (p. 375) report on the worms found in an investigation of labourers at São Caetano, Brazil. Hookworm infection was fairly common and *S. mansoni* was found in a number of cases.

Discussing bilharzial affections of the appendix, MOHAMED (p. 40) draws a distinction between the bilharzial appendix, in which eggs are found in the tissues, with infiltration by active cells of the reticulo-endothelial system, and bilharzial appendicitis, in which bacterial infections are superimposed. He points out that in his autopsy specimens the infestation was never confined to the appendix, but was usually severe in the intestine or urinary tract or both. On the other hand, 17 per cent. of a series of appendices removed at operation were normal, and he considers that the symptoms which led to operation were probably caused by bilharzial infection of the intestine or urinary tract, and that permanent cure could have been effected by antimony, or other anthelmintic treatment, after infection had been diagnosed by the usual means.

He further states that bilharzial infection of the gall bladder does not occur in isolated or primary form, and that secondary bacterial infection may take place. The proper treatment of the worm infection is by drugs. Ova may be found in the submucosa or muscular layers or in the subserous coat, but he does not consider that eggs may form nuclei for gallstones. In view of the fact that 21·9 per cent. of gall bladders removed after the diagnosis of chronic cholecystitis were normal in appearance, he advises that when investigations in such cases point to bilharzial infection, the patient should be treated with drugs. In this way he believes that most cases would be permanently cured.

ROBERTSON (p. 42) reports endemic infection with *S. japonicum* in the West Yunnan plain, where infected snails of the *Katayama* group were found in irrigation ditches.

YAO (p. 43) describes a focus of *S. japonicum* infection in the Kwangsi Province of southern China, in which 55 per cent. of a random sample of the population were infected. Oncomelania snails (but not

nosophora or *lupensis*) were collected from streams and irrigation ditches and 7·8 per cent. harboured the cercariae, which were infective for experimental rabbits.

Wu (p. 43) has shown that in China the following animals have been found infected with *S. japonicum*: sheep, goats, house rats, dogs, cats, oxen, buffaloes and horses. He thinks that field rats may be infected in the endemic areas, and although pigs have not been found naturally infected, they are susceptible to experimental infection. He notes that in the Yangtse delta the faeces of sheep and goats are used to fertilize the land, and points out that this practice constitutes a risk to man. Control of infection in man and animals must take into account these reservoir hosts.

Garcia *et al.* (p. 43) found eggs of *S. japonicum* in the tissues of a chronic ulcer of the leg of a child in the Philippines; eggs were also present in the faeces.

Brackett (p. 44) describes the features governing the occurrence of schistosome dermatitis in Wisconsin; he points out that this condition is not serious. Cort *et al.* (p. 44) give reasons for the belief that the cause of schistosome dermatitis at the bathing beaches of Michigan is *Cercaria stagnicolae*, a parasite of the snail *Stagnicola emarginata*.

Brackett (p. 378) gives an account of the pathology of schistosome dermatitis, as seen in portions of excised skin. The cercariae do not, apparently, penetrate beyond the epithelial layer. He has exposed his own skin to the cercariae (*C. elvae* and *C. stagnicolae*) on many occasions, and notes that it has become increasingly sensitive, the later exposures producing almost immediate urticarial response. In persons who show no reaction to the cercariae it is thought that they do not enter the skin.

The same author (p. 379) discusses the biology of the snail hosts of the cercariae of schistosome dermatitis in Wisconsin. The incidence of the dermatitis is determined by the life history of the snails; *Stagnicola emarginata* dies off about August, and *Physa parkeri* at an earlier season; at these times the infection begins to disappear.

Other trematodes.—Komiya and Tajimi (p. 44) describe the structure of the cercaria and metacercaria of *Clonorchis sinensis*. In the Shanghai area the first intermediate host is *Bithynia striatulus*, and in the same area two additional second intermediate hosts have been confirmed, *Leucogobio polytaenia* and *Squaliobarbus curriculus*. Hsü and Li (p. 380) show that *Bithynia longicornis* is a first intermediate host of *C. sinensis* in the Canton area, which is an endemic centre of infection.

Invasion of the pancreas by *C. sinensis* has been found quite frequently in Japan, and Galliard *et al.* (p. 45) now report two cases from Tonking. The clinical findings and pathological changes are described; both patients died.

Sandground (p. 382) reports that he found a single worm of the genus Plagiorchis in the contents of the small intestine of a native of Java. This is the third occasion on which a trematode of this genus has been found in man; he has named it *Plagiorchis philippinensis* because the first record came from the Philippines.

Wu (p. 46) gives an account of the geographical distribution of paragonimiasis in China, and of the reservoir hosts—rat, dog, cat, wild cat, leopard and tiger. Of the intermediate hosts Melania and Potamon live in mountain streams, Assiminea and Sesarma in delta regions. The eating of crabs is common, and in many places they are not cooked,

but are placed in wine for 12 hours or even less. Encysted metacercariae may be viable in these wines for 18 to 43 hours, and in some wines even the crabs themselves are not killed, but are sold as "drunken" crabs and eaten in that state.

In the Sintiku Prefecture of Formosa the incidence of infection with *Paragonimus westermanii* is 5·53 per cent. among children of the aboriginal Takasago race. KINUGASA (p. 45) considers that infection is chiefly due to the eating of uncooked *Potamon rathboni* and *P. dehaanii*.

TANG (p. 381) differentiates two types of Paragonimus in Fukien Province, the *ringeri* type and the rodent type. Of the *ringeri* type the first host is *Melania toucheana* and the second *Potamon denticulatus*; of the rodent type *Katayama tangi* and *Parathelphusa sinensis*.

YOKOGAWA *et al.* (p. 47) obtained encouraging results in the treatment of dogs infected with *P. westermanii* by means of injections of Prontosil soluble, 2·5 per cent., and emetine hydrochloride. They describe the effects of this treatment on the eggs of the fluke. They tried the treatment in 9 human cases, giving total doses of 60–165 cc. Prontosil intramuscularly and 12–23·5 cc. emetine hydrochloride (4 per cent.) intravenously over a period of 7–17 days. The results appeared to be good in 4 cases followed up for 5 months, 2 patients were lost sight of, 1 died of unrelated disease, and 2 relapsed with severe haemoptysis.

STIGLICH (p. 383) notes that in 4 cases of *F. hepatica* infection eggs could be found by means of a duodenal sound, but were present in the faeces of one patient only. There was epigastric colic and an icteric tinge in the sclera; in one there was eosinophilia. Emetine hydrochloride was apparently valuable in treatment.

MANSON-BAHR and WALTON (p. 382) report the finding of a specimen of *Fasciola hepatica* in the common bile duct of a woman in Britain; they note that eggs could not be found in the faeces. This is apparently the second case of removal of this fluke from the common bile duct; the symptoms which led to operation suggested pancreatitis.

In Bogotá, Colombia, BRUMPT *et al.* (p. 48) have incriminated *Limnaea bogotensis* as an intermediate host of *Fasciola hepatica*.

WU (p. 48) refers to infection with *Fasciolopsis buskii* in China, and mentions as intermediate hosts *Segmentina calathus*, *Hippeutes cantori*, and *Cyraulus saigonensis*, which are not usually included in text-books.

SANDGROUND and BONNE (p. 383) describe the morphology of *Echinostoma lindoensis*, a parasite of man in Celebes. At Lake Lindoe larval development is found in the small planorbid snail *Anisus* (*Gyraulus*) *sarasinorum*, and metacercariae in pulmonate snails *e.g. Viviparus javanicus rudipellis* or in the mussel *Corbicula lindoensis*. These mussels are freely eaten by the natives and human infection is proportionate to the distance from the lake; experimentally man has been successfully infected by eating the mussels; treatment with tetrachlorethylene is effective.

LARIOS RODRIGUEZ (p. 383) describes 5 cases of human infection with *Echinostoma revolutum* in Mexico; the symptoms included intense abdominal pain and diarrhoea, with eosinophilia and anaemia. In treatment hexylresorcinol is effective. The intermediate hosts are *Limnaea attenuata*, *Physa osculans* and *Planorbis tenuis*.

BEAVER (p. 384) gives an account of the life history of *Euparyphium melis*, of which the first intermediate host is a snail, *Stagnicola emarginata angulata*, and the second a tadpole. HSÜ (p. 384) reports the finding of two specimens of Euparyphium in the small intestine of a

Chinese in Peiping ; these were probably identical with *E. melis* and it is suggested that the patient became infected by ingesting tadpoles.

Cestodes.

BONNE (p. 470) gives a brief account of the seven tapeworms found in man in the East Indies, *T. saginata*, *T. solium*, *D. caninum*, *H. diminuta*, *H. nana*, *Raillietina madagascarensis* and *Bertiella studeri*. He (p. 473) records a case of the last in a Chinese girl in Java.

BARNETT (p. 471) gives an account of the incidence of hydatid disease in New Zealand and in other countries. The alveolar form is almost confined to Bavaria, Tyrol, Wurtemburg, Switzerland, Moscow, Kasan, Irkutsk and Tomsk. DÉVÉ (p. 471), however, reports a case of ordinary hydatid, together with alveolar hydatid, in a native of Normandy whose only residence away from home had been in Salonika during the war of 1914–1918.

HAIGHT and ALEXANDER (p. 111) state that hydatid disease has occurred in only five persons known to have been born in the United States, but the infection is not rare in swine, especially in the south.

WILLIAMS (p. 111) reports, for the first time in Szechwan, W. China, infection of a dog with *E. granulosus*.

ROSE and CULBERTSON (p. 111) have confirmed the group specificity of the Casoni and Ghedini-Weinberg reactions in hydatid disease. Antigens from other cestodes may be substituted for hydatid fluid in the skin test or in the complement fixation test.

STUNKARD (p. 113) states that *Bertiella studeri* utilizes free-living mites as intermediate hosts, and gives the names of some of them.

BONNE and MREYEN (p. 112) have found *Raillietina madagascarensis* for the first time in man in the Malayan Archipelago (Java) ; no indication of the mode of infection could be obtained. The characters of the worm are described.

KOURÍ and RAPPAPORT (p. 113) record the finding of 18 human infections with a species of Inermicapsifer in Cuba. It was found in children only, gave few if any symptoms and was easily expelled by means of male fern, carbon tetrachloride or coconut oil. A description is given.

BONNE and LIE KIAN JOE (p. 469) report the finding of two spargana in the wall of the jejunum of a man in Java ; they developed to maturity when ingested by a kitten and proved to be of the genus Diphyllobothrium, subgenus Spirometra. *Charles Wilcocks.*

[*To be continued.*]

MALARIA.

CARR (Henry P.) MELÉNDEZ (Joaquín Fernández) & MELÉNDEZ (Aristides Fernández). **Malaria Reconnaissance of the Province of Camaguey in Cuba.**—*Amer. Jl. Trop. Med.* 1941. Nov. Vol. 21. No. 6. pp. 739–750. With 1 map.

The Camaguey Province of Cuba coincides with the Great Camaguey Plain and is made up of plains or rolling open country, broken by occasional hills and by a few low mountains. Most of the Province is free of hills ; those that exist are chiefly to be found in the north-east part near the border of Oriente Province. The province extends right

across the island from sea to sea. The northern part and most of the central portion has soil composed of heavy clay which is more or less impermeable. The soil of the southern portion is light, mostly covering limestone ; here the drainage is good.

The population is composed of 297,000 whites and 111,000 negroes.

Nearly all schools in the Province were visited : 7,068 children were examined for enlargement of the spleen, and blood examinations were made of 3,374. The latter included all children having enlarged spleens and so was to that extent a selected group. The percentage with enlarged spleens was 18 for whites and 7 for negroes. Of blood films examined 0·5 per cent. contained parasites among the white children, 1 per cent. among the negroes. The spleen indices in different municipalities varied from 7 to 32. The areas of highest malaria endemicity are those with the poorest natural drainage. In Camaguey city endemic malaria is confined to the outskirts where borrow-pits supply facilities for mosquito breeding.

P. vivax was found three times more frequently than *P. falciparum* ; *P. malariae* was not seen. Low parasite rates with considerable splenomegaly indicate that malaria has not recently been active. The last malaria epidemic in the Province was in 1934. The abandonment of the practice of importing labour for the cane harvest has probably reduced epidemic malaria in Cuba in recent years. *A. crucians*, *A. vestitipennis* and *A. albimanus* were found breeding ; the first two were relatively rare. *A. albimanus* is the important vector.

The malaria conditions are similar to those found by the authors in Oriente Province [see this *Bulletin*, 1940, Vol. 37, p. 664].

Norman White.

CARR (Henry P.) & MELÉNDEZ (Joaquín Fernández). **Malaria Reconnaissance of the Province of Pinar del Rio in Cuba.**—*Amer. Jl. Trop. Med.* 1942. Jan. Vol. 22. No. 1. pp. 51–61. With 1 map.

This is a further instalment of the report on the malaria survey of the Republic of Cuba. Pinar del Rio Province is the most western of the six political divisions of the Island. The Organ mountains lie almost wholly in this Province, dividing it into a narrow northern and a broader southern coastal plain ; the maximum breadth of the latter is some 20 miles. Creeks and rivers are numerous in the south. As in other provinces investigations were largely confined to school-children [see summary of report on Camaguey Province above].

The population of Pinar del Rio is 343,482, of whom 270,547 are white, 72,935 are negro. The spleen rate of 13,830 white children was 14, and of 3,025 negroes 3. Malaria parasites were found in only 33 films ; 7,407 were examined. *P. vivax* was found in 20, *P. falciparum* in 13. The highest degree of malaria endemicity is found in the portion of the coastal plain which lies at a lower elevation than 100 feet. Epidemic malaria may occur ; there was an epidemic in 1934, attributed to unusually heavy rainfall and bad economic conditions following the depression.

Anopheline larvae collected were identified as *A. crucians*, *A. vestitipennis*, *A. grabhami* and *A. albimanus*. *A. albimanus* predominates throughout the coastal area and is most prevalent at elevations of 100 feet or less. It is most numerous during the season of most active malaria transmission.

A. vestitipennis may be of some importance as a malaria vector in some parts of Cuba, but *A. albimanus* is the important vector of that country. *Norman White.*

CARR (Henry P.), MELÉNDEZ (Joaquín Fernández), ROS (Alberto) & MELÉNDEZ (Arístides Fernández). **Malaria Reconnaissance of the Province of Havana in Cuba.**—*Amer. Jl. Trop. Med.* 1942. Jan. Vol. 22. No. 1. pp. 63–71. With 1 map.

Havana is the smallest of the six provinces of Cuba. It lies between the Pinar del Rio and Matanzas Provinces. It covers 3,254 square miles and is divided into 26 municipalities or counties. The total population is 985,500, and of these 774,518 are white, 210,982 negro or mixed. Most of the Province is flat or undulating. There are a few hills in the west, outlying hills of the Organ mountains of Pinar del Rio, and there are a few hills 300 to 400 feet high east and south-east of Havana city. The plain has a sublayer of porous limestone. The soil is deep red Matanzas clay, fine and permeable. Surface drainage is excellent; ponds and lakes are infrequent. Mangrove swamps along the north and south coasts, if free communication with sea water be prevented by sandbars, may produce *A. albimanus* in abundance. The flat valley of the Almendares River has comparatively impervious soil on which rain water and irrigation water may collect and provide breeding facilities for *A. albimanus*. Old borrow pits that have become silted and puddled may contain water for considerable periods during the rainy season.

Nearly every school in the Province, outside Havana city, was visited. The number of children examined was equivalent to 2·2 per cent. of the total population outside the city, and in the city to 1 per cent. of its population. The spleen rate of 15,940 white children was 9; of 3,248 negro children 3. Only two positive blood films were found among 9,982 examined; both these were from children living near the Almendares River valley. Very few schools had spleen rates as high as 21 per cent. There is very little endemic malaria in Havana Province at present; this is probably explained by the porous nature of the soil and subsoil. As in other Provinces of Cuba *A. albimanus* is the dominant species found breeding. Breeding places other than the three types mentioned above were scarce. A few larvae of *A. crucians*, *A. vestitipennis* and of *A. grabhami* were also found.

Norman White.

GORDON (R. M.), DAVEY (T. H.) & PEREGRINE (E. P.). **A Mechanical Trap for sampling Mosquito Populations entering Houses.**—*Ann. Trop. Med. & Parasit.* 1941. Dec. 31. Vol. 35. No. 2. pp. 269–276. With 3 figs. [19 refs.]

After reviewing the methods that have been used to estimate the numbers of mosquitoes entering a house during the night, the authors describe with full constructional details a new type of trap designed to be fitted into a single open window of a room. In principle the trap consists of a screen of mosquito-netting in the form of a roller-towel held taut between an upper and lower roller. The upper roller is kept revolving by a small motor worked from a 12 volt storage battery; and as the netting is carried slowly upwards at a rate of 5 ft. per minute, the mosquitoes alighting on it are swept off into a small

container from which they can be collected in the morning. The ability of the trap to catch mosquitoes has been proved, but it has not yet been given an extensive trial. *V. B. Wigglesworth.*

LEESON (H. S.). **The Occurrence of *Anopheles marteri* in Syria.**—*Bull. Entom. Res.* 1942. Apr. Vol. 33. Pt. 1. pp. 35–37.

In this paper, besides a description of *A. marteri*, is given a useful key to the adults and larvae of the seven species of Anopheles so far found in Syria : *A. sacharovi*, *A. hyrcanus*, *A. superpictus*, *A. sergenti*, *A. claviger*, *A. marteri* and *A. algeriensis*. *C. W.*

SICART (Marcel). Contribution à l'étude des anophèles de Tunisie. Présence de *Anopheles* (*A.*) *claviger* (Meigen 1884). [*A. claviger* **in Tunisia.**]—*Arch. Inst. Pasteur de Tunis.* 1941. Dec. Vol. 30. No. 3–4. pp. 287–290. With 1 fig.

RAMOS (A. da Silva) & UNTI (Ovidio). Notas sôbre os anofelinos de São Vicente e suas imediações. [**The Anopheles of São Vicente.**]—*Arquivos de Hig. e Saúde Pública.* São Paulo. 1940. Sept. Vol. 5. No. 10. pp. 53–61. With 4 figs. on 2 plates. English summary (5 lines).

PARISE (N.) & LUCREZI (G.). Ricerche sulla malaria cronica. [**Research on Chronic Malaria.**]—*Riv. di Malariologia.* Sez. I. 1941. Sept.–Oct. Vol. 20. No. 5. pp. 301–308. With 3 figs. (1 coloured) on 1 plate. [25 refs.] French summary (8 lines).

The hypothesis that malaria is primarily a disease of the reticulo-endothelial system was the basis of the observations described in this paper, which were intended to throw light on the nature of chronic malaria. Seventy-six cases of chronic malaria were studied ; in 60 the disease was latent ; the remainder were relapsing cases. Nearly all the patients had contracted malaria in Africa ; all had been intensively treated with quinine. For the most part the study was confined to an examination of material obtained by spleen puncture ; all the patients had enlargement of the spleen. In five cases sternal puncture was carried out, and in two the liver was punctured.

In all cases there was evidence of hyperactivity of the reticulo-endothelial system ; this varied in degree and was most marked in the few cases in which malaria parasites could still be demonstrated. There was a great increase in very young forms of blood cells. There was evidence of marked phagocytic activity ; endothelial cells englobing detritus of various kinds, red cells, leucocytes, malaria pigment and sometimes parasites, were commonly seen. No non-pigmented free forms of malaria parasite were found, or rather none that could be certainly identified as such. The authors stress the difficulty of the search for such non-pigmented forms and the possibilities of error in their identification. *Norman White.*

MAILYAN (L. M.). [**Oedema of the Lungs of Malarial Origin.**]—*Sovet Med.* Moscow. 1941. No. 4. pp. 12–13.

The author notes that the respiratory organs are rarely affected in malaria, and refers to the few cases of pneumonia ascribed to malaria which have been reported in the literature. He gives an account of two of his own cases, in which pulmonary oedema appeared during

attacks of subtertian malaria, subsiding after anti-malarial treatment. In neither case was any other cause of the oedema found, and the close association of the two conditions, in onset and course, is strong evidence that they were causally connected.

The first patient was a man of 18 who had lived in a non-malarious area but had recently travelled through a malarious region near Baku; he was comatose on admission, *P. falciparum* was found in his blood, there was intense dyspnoea, with bubbling râles, impaired percussion note at the bases, frothy sputum but a clear X-ray picture. The chest condition cleared completely after quinine, atebrin and plasmoquine treatment. The second patient was aged 16; his history and symptoms were much the same, and the condition cleared after the same treatment.

It is noteworthy that both patients were young and that in both cases the pulmonary oedema accompanied the first attack of malaria; it is therefore possible that the oedema was associated with a non-immune state. The effect of anti-malaria treatment was striking.

V. C. Robinson.

ZIKEYEV (V. V.). [**Trophic Disturbances in Malaria.**]—*Sovet Med.* Moscow. 1941. No. 4. p. 14.

Prolonged malarial infection leads to progressive anaemia and increasing melanosis due to uptake of melanin by the cells of the reticulo-endothelial system. This lowers the biological stability of the tissue and renders it especially vulnerable to exogenous stimuli. The author describes certain skin conditions in which there were trophic disturbances which he ascribes, without doubt, to malaria. One was a case of indolent ulcer of the heel, three were of gangrene of the penis or scrotum; there was evidence of malaria in all. Anti-malarial treatment appeared to produce a definite effect on all these ulcers, which healed in three to four weeks.

The author mentions the case of a girl who had a facial disfigurement due to an accident. Skin grafting had been attempted unsuccessfully until it was noticed that attacks of malaria followed each operation. The patient was therefore given quinine before each succeeding operation, with the result that the grafts took and the whole area was successfully covered.

V. C. Robinson.

GRACHEV (Y. S.). [**Combined Treatment of Malaria with Akrichin and Biochinol.**]—*Sovet. Med.* Moscow. 1941. No. 4. p. 16.

Akrichin [atebrin] by the mouth administered alone is unsatisfactory in malaria, since, although it cuts short the attack, it does not prevent recurrence. In 1939 akrichin hydrochloride hypodermically was tried at Kuibyshev, but again the attacks recurred.

A combined course of akrichin and biochinol was therefore worked out as follows: akrichin 0·1 gm. *per os.* was given three times a day for five days; on the fourth, seventh and tenth days injections of biochinol 0·3 gm. were given.

Biochinol contains iodine, quinine and bismuth and forms a depot from which quinine and iodine are gradually released into the circulation. At Kuibyshev the treatment has been successful both in cutting short the malarial attack and in preventing recurrence.

V. C. Robinson.

LOPATIN (G. M.). [**Diagnosis and Laboratory Investigation of Malaria in Children.**]—*Trans. Kuibyshev Milit. Med. Acad. Red Army.* 1940. Vol. 4. pp. 203–213. [In Russian.]

This paper deals with the peculiarities of malaria in children and their influence on diagnosis. It is pointed out that the diagnosis of malaria in children presents great difficulties owing to variations in the clinical course, and atypical manifestations. For example, during attacks in small children it is easy to overlook the cold stage, since it is not always pronounced and may even be absent. In many children rigor is accompanied by vomiting, while in some cases there may be involuntary micturition. In the hot stage the temperature curve may be irregular, pyrexia appearing too early or too late, while its duration is either too short or too long. These irregularities may lead to wrong diagnosis and to confusion with other febrile conditions. As to the sweating stage, it is frequently absent or inconspicuous in young children. The importance of spleen enlargement in malaria is diminished owing to the frequency of splenomegaly in children due to other causes (rickets, Banti's disease, leishmaniasis, etc.). Though the only infallible method of diagnosis is the finding of the parasites in the blood, these could not be found in many cases of undoubted malaria, the parasitic index in children attending the clinic being only 65. Among changes in the blood, variation in the number of platelets appears to be significant. It falls considerably in the course of the disease (sometimes to 25,000) but gradually increases during treatment; thrombocyte counts are, therefore, recommended as a guide to the efficacy of treatment. The author also considers the sedimentation rate of red corpuscles to be of diagnostic value. It rises as the disease progresses but falls rapidly during treatment, reaching the lowest level when parasites disappear from the circulation. Unless the sedimentation rate falls to the normal level malaria is not regarded as cured. The rate was found to be highest in benign tertian, lowest in subtertian and intermediate in quartan. The last part of the paper is devoted to metabolism in malaria. *C. A. Hoare.*

LOPATIN (G. M.). [**Congenital Malaria.**]—*Trans. Kuibyshev Milit. Med. Acad. Red Army.* 1940. Vol. 4. pp. 215–221. [In Russian.]

The author first briefly reviews the case for congenital malaria. With regard to the mechanism of infection, transplacental transmission is considered to be the only possible method. This may be (1) intrauterine, produced by the emigration of infected maternal erythrocytes into the foetus as the result of damage to the placental vessels caused by malaria; or (2) at the time of parturition, during the detachment of the placenta, which may be accompanied by rupture of some of the villi and lead to the mixing of the maternal and foetal bloods.

After describing the influence of malaria upon the pregnant mother and foetus, the author passes to a review of 35 cases of congenital malaria observed in Kuibyshev. In determining the antenatal nature of the infection in infants the following criteria were used: (1) presence of malaria attacks in the mother during pregnancy, or immediately before or after parturition; (2) manifestation of malaria in the infant within an interval not exceeding the incubation period (about a fortnight); (3) appearance of first symptoms of malaria between November 1st and April 1st, *i.e.* during the season of inactivity of mosquitoes; and (4) finding of the same species of Plasmodium in mother and infant.

With respect to type of malaria, the cases were distributed as follows: 15 benign tertian, 10 subtertian, 8 quartan. In 27 cases the weight of the new-born infants was under 3,000 gm., 15 being below the lower limit for full-term infants (2,500 gm.). Chronic disturbances of nutrition appear to be a common feature in congenital malaria. The fever was erratic in 24 cases; the attacks were quotidian or on alternate days in eight cases and absent altogether in three. Spleen enlargement was more marked than in acquired malaria. The complexion of infants suffering from congenital malaria is characteristic and may serve as an early diagnostic character. The skin is usually very pale, waxy or earthy, sometimes even jaundiced. The haemoglobin content falls to 20 per cent., red blood cells to 1 million, there is leucopoenia, and other blood changes found in malaria are present. In congenital malaria the jaundiced complexion and blood changes are more persistent under treatment than in acquired malaria. The pathologico-anatomical changes are identical with those in chronic malaria, with large accumulations of pigment in the spleen, liver and other organs.

Congenital malaria is usually refractory to treatment with quinine and acriquine [atebrin], and it may leave a lasting effect in the subsequent life of the child, in the form of infantilism and low resistance against infections and environmental influences. *C. A. Hoare.*

SABLIN (P. E.) & EGOROVA (O. G.). [**Peculiarities in the Course of Lobar Pneumonia in Malarial Patients.**]—*Trans. Kuibyshev Milit. Med. Acad. Red Army.* 1941. Vol. 5. pp. 23–27. [In Russian.]

A comparison of cases of lobar pneumonia with those in which this disease was combined with malaria, has demonstrated the following facts: (1) Malaria affects the reactive faculty of the organism, thereby influencing the course and issue of lobar pneumonia; (2) the clinical course of this disease in malarial patients is characterized by the frequent absence of leucocytosis and by a retardation of the resolution of the process, resulting in prolongation of the fever period and in belated disappearance of the signs in the lungs detectable by percussion and auscultation; (3) the reduced reactivity of the organism in malarial subjects may lead to complications in lobar pneumonia (carnification of the lung, suppurative processes, etc.). *C. A. Hoare.*

ORLINA (M. M.). [**Functional Changes of the Liver in Malaria.**]—*Trans. Kuibyshev Milit. Med. Acad. Red Army.* 1941. Vol. 5. pp. 29–34. [In Russian.]

The author describes changes in the function of the liver observed in malaria. She notes that enlargement of this organ is just as frequent as enlargement of the spleen (41 in 47 cases). The functional state was studied by determining the bilirubin and carbohydrate metabolism, and the condition of the active mesenchyme. Bilirubinuria and bilirubinaemia were found respectively in 22 and 18 per cent. of subtertian cases, in 33 and 61 per cent. of benign tertian, and in one out of three cases of quartan. Urobilinuria, reflecting hepatic insufficiency, occurred in 25 per cent. of subtertian cases, 60 per cent. of benign tertian and in two out of three cases of quartan. The condition of the active mesenchyme was determined by the rate of excretion of methylene blue (introduced intramuscularly) by cells of the reticulo-endothelial system. An increased rate was found in 12 out of 14 cases. As regards the carbohydrate

metabolism, it was slightly disturbed in the acute cases, in 50 per cent. of subtertian and quartan, and in 60 per cent. of benign tertian, while simultaneous disturbances in all the hepatic functions in question were observed in 25 per cent. of cases. Finally it is noted that in the Kuibyshev district malarial cirrhosis of the liver is a common occurrence. *C. A. Hoare.*

BYSTRITSKI (I. A.). [**Nephropathies in Malarial Children.**]—*Trans. Kuibyshev Milit. Med. Acad. Red Army.* 1941. Vol. 5. pp. 35–39. [In Russian.]

In Kuibyshev the author observed nephropathies in 55 out of 300 (18·3 per cent.) cases of malaria in children dealt with in 1938 and 1939. The frequency of kidney disorders was greatest in subtertian, after which came quartan and benign tertian malaria. The majority (35) were cases of pyelitis, while nephroso-nephritis was observed in 18 patients, and pure nephrosis in two. Most of the cases of nephropathy (34) were mild and responded readily to specific quinine therapy, good hygiene and dietetic treatment. In some cases, however, there occurred medium (12) and severe (5) forms of malarial nephropathy, producing persistent changes in the renal tubules, or eclamptic, pseudo-uraemic symptoms. *C. A. Hoare.*

DE NEGRI (Ugo). Frequenza e interpretazione diagnostica delle granulazioni basofile degli eritrociti nel sangue di malarici, privo di parassiti. [**Frequency and Diagnostic Significance of Basophile Granulations of Red Cells of Blood of Malaria Patients from which Parasites are Absent.**]—*Riv. di. Malariologia.* Sez. I. 1941. Sept.–Oct. Vol. 20. No. 5. pp. 309–316. With 1 fig. [15 refs.] French summary (7 lines).

The author has noted the frequency with which basophile granulation of parasite-free red cells is seen in the blood of malaria patients, both in the presence and absence of such parasites in the peripheral blood. For staining blood films the method of May-Grünwald-Giemsa is used. Notes on the results of examination of 1,400 blood films are given. In 222, basophile granulation was seen but no malaria parasites were found; in 55, ring forms of *P. falciparum* were found with basophile granulation of non-parasiticized red cells; in 30, crescents were found with similar granulation of parasite-free cells. Similar findings were reported in 12 films containing young forms of *P. vivax* and in five containing *P. vivax* gametocytes. These granular cells are commonly normal in size, the number of granules is 10 to 20, and one such granular cell may be found in from 15 to 20 microscope fields.

To 78 of the 222 patients, parasite-free but with basophile granulation, adrenalin was given to provoke splenic contraction. During the ensuing febrile attacks *P. falciparum* was found in the blood of 38, *P. vivax* in the blood of 15. In 25 there was no thermal or parasitic response to the adrenalin.

The author concludes that such basophile granulation is of very considerable diagnostic significance if parasites cannot be found. Its presence indicates in his experience that there is a 70 per cent. probability of a *P. falciparum* infection. *Norman White.*

VINCI (Achille). Sindrome addominale acuta da malaria. [**Acute Abdominal Syndrome in Malaria.**]—*Riv. di Malariologia.* Sez. I. 1941. Sept.–Oct. Vol. 20. No. 5. pp. 341–348. [16 refs.] French summary (4 lines).

This is a description of a patient admitted to hospital with nearly all the signs and symptoms of an acute abdominal lesion, intense pain, distension, generalized tenderness, bilious vomiting, constipation, rapid pulse and respiration. The pulse was not, however, the small thready pulse of a generalized peritonitis. There was, after a period of acute distress, a certain rhythm in the severity of the symptoms synchronous with febrile manifestations, which indicated the possibility of a malaria infection. An injection of adrenalin caused the appearance of *P. falciparum* in the peripheral blood. Quinine effected a cure. The paper contains numerous references to comparable cases in the literature.

Norman White.

VINCI (Achille). Eruzione esantematica di origine malarica. [**Exanthematic Eruption of Malarial Origin.**]—*Riv. di Malariologia.* Sez. I. 1941. Sept.–Oct. Vol. 20. No. 5 pp. 349–352. [11 refs.] French summary (3 lines).

The description of a patient with a diffuse rash covering the abdomen and back and to a less degree the thorax. The face, hands and feet were free. The rash consisted of oval rose-coloured spots the size of a bean ; it was not confluent and but little irritable. An intravenous injection of 1/20 mgm. of adrenalin was followed by the appearance of *P. falciparum* in the peripheral blood. The patient had received no anti-malarial treatment before the appearance of the rash. The author regards the rash as an indication of sensitivity to toxins elaborated by the malaria parasites. *Norman White.*

FRICKS (L. D.). **Emergency Measure and Foresight in Malaria Control.** —*Milit. Surgeon.* 1941. Aug. Vol. 89. pp. 182–188. [Summary taken from *Public Health Engineering Abstr.* Washington. 1941. Dec. Vol. 21. No. 12. p. 15. Signed Harold F. ROCK.]

The word " foresight " in the title is particularly applicable to this paper because it was originally published in the August 1920 edition of " The Military Surgeon." The conditions prophesied have come into being in the present emergency.

The article indicates that the routine measures against malarial mosquitoes be employed, but, with the use of construction camps and rapidly built camps, it is often some time before the usual measures can become effective. It is emphasized that, in selecting a camp site, bodies of water that are apparently nonpotential sources of Anopheles production should be carefully examined to see if seasonal floatage or aquatic vegetation may cause potential mosquito breeding places at certain periods.

Mosquito nets are markedly ineffective. Salves and lotions are effective only for comparatively short periods. A study of life habits of Anopheles shows that their habits may be used to advantage in their destruction.

(1) After becoming engorged, they rest on the wall or other shaded resting places relatively close to where they obtained their blood meal.

(2) Those who have digested their meal are most apt to depart from the enclosure or house either just after dusk or soon after daylight.

(3) In a screened building those ready to depart collect on the door or window screens where they may easily be destroyed.

(4) Recently engorged mosquitoes at rest are easily destroyed with an ordinary fly swatter.

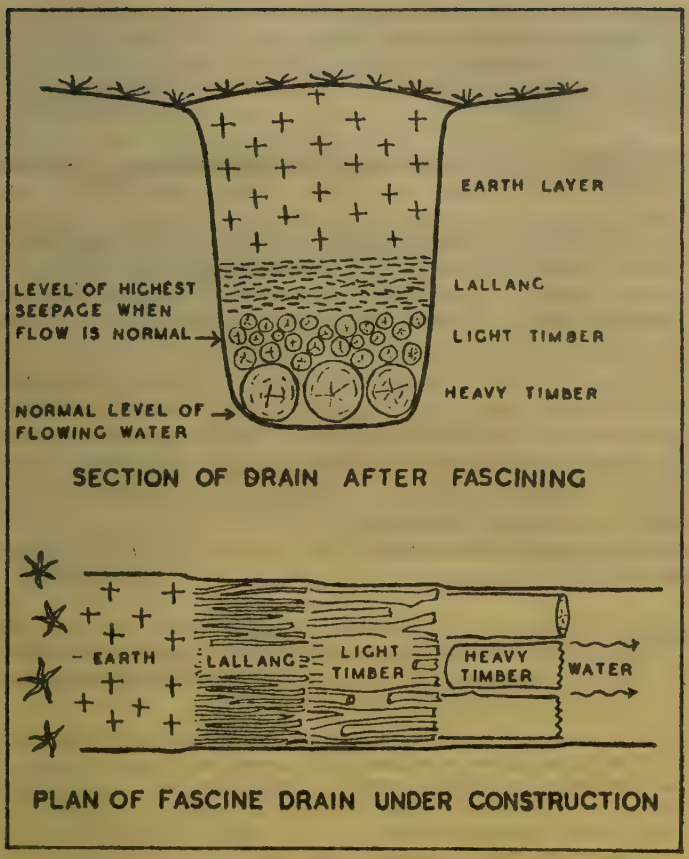
(5) Light-coloured walls make their destruction an easier task. On dark surfaces or in relatively dark rooms, a flash lamp is an advantage.

Gorgas made practical application of this method at the Panama Canal construction with excellent results. In two camps 200 yards apart, near a swamp, one employed this method, and the other did not. The malaria rate was 42 times higher in the camp not employing this control measure.

The fact that the destruction of engorged mosquitoes is successful as a control measure depends on the fact that at its first bite the mosquito never carries but receives infection, and it is only after the lapse of a week or more that it becomes capable of infecting a human host at a subsequent bite. Hand catching or destruction of engorged mosquitoes is simple and has been proven to be effective if efficiently carried out.

TWEEDIE (D. Reid), REID (J. A.) & HODGKIN (E. P.). **Fascine Drainage.** Prepared for the Malaria Advisory Board, F.M.S., Kuala Lumpur. 14 mimeographed pp. With 2 figs. [1941].

This pamphlet explains the technique of fascine drainage. The method described has given satisfactory results in small watercourses which are the most important breeding places of *A. maculatus*. The drain is first cleaned thoroughly by removing vegetation and all obstructions. Packing starts at the head of the drain. The size of the wood will depend on what is available and on the size of the drain ; the bigger the drain the bigger the timber. For large watercourses whole tree-trunks can form the bottom layer. The details of construction are well shown in the illustration. The logs should overlap one another slightly. Instead of lallang, palm fronds, shrubbery or thick grass may be used. The packing is protected with a covering of earth usually obtained by cutting from the sides of the drain ; this should not be less than one foot thick. In very deep drains it may not be necessary to fill to ground level. Vegetation must be encouraged to grow over the drain with all speed. It is important to complete one portion of the drain at a time, otherwise it may become choked before completion. Tributaries must be fascined before the main channel and should enter the main drain pointing downstream. Sharp bends should be avoided. The amount of timber used will depend on the volume of water to be drained ; the amount should be increased gradually from source to outlet. It is important to protect newly fascined drains from damage by storm water. In swampy soil newly cut drains should be left open for a month before fascining and so acquire a normal level of water. If water entering a fascined drain contains much silt it can be passed through a stone-packed filter. Sullage should be similarly treated if it be taken into a fascined drain.



Norman White.

EJERCITO (Antonio). **Atabrine in Malaria Prophylaxis.**—*Riv. di Malariologia.* Sez. I. 1941. Sept.–Oct. Vol. 20. No. 5. pp. 317–328.

The author reports the results of an attempt to determine the value of atebrin as a prophylactic of malaria. A labour force working on the Manila-Ipo aqueduct in the Philippines, in an endemic malaria area in which no attempt was made at Anopheles control, was the subject of experiment. The labour force was imported and some members of it stayed for very short periods. A preliminary spleen and blood survey determined those who had no evidence of malaria infection, and no history of previous malaria attacks. Of these 212 were given atebrin, 0·20 gm. twice a week; 272 received no prophylactic treatment. Otherwise the conditions of the two groups were comparable. The observations were continued for about 11 months. Of the 212 members of the atebrin group only 78 " sticked to the place from the

minimum of eight days to the maximum 300 days (averaging 41 days)." Of these 10 contracted malaria, 13 per cent. Of the control group 106 remained for periods of from 8 to 150 days, (average 23 days); of these 38 acquired malaria infection, 36 per cent. A protocol contains details of each individual. *Norman White.*

DIKSHIT (B. B.). **Malaria Immunity in the Rhesus Monkey.**—*Jl. Malaria Inst. of India.* 1941. Dec. Vol. 4. No. 2. pp. 199–206.

The elaboration of a method of transferring the blood of one monkey to another has enabled the authors to study the effect of transference of blood of monkeys immune to *Plasmodium knowlesi* infection to non-immune monkeys. When about 80 per cent. of immune blood was withdrawn from an immune monkey and was replaced by non-immune blood the monkey did not lose any of its immunity to superinfection. If over 70 per cent. of the blood of a normal monkey was withdrawn and replaced by immune blood the monkey acquired an immunity. If this last experiment were performed with an infected instead of a normal monkey the infected monkey was cleared of most of its infection, the animal passing into a state of chronic infection. The results of these experiments are discussed from the point of view of the mechanism of immunity in malaria and it is concluded that the cellular and humoral factors are working together in close co-operation, the humoral agencies probably acting by stimulating the cells and not directly on the malarial parasites. *C. M. Wenyon.*

SEETHARAMA IYER (P. V.), SHORTT (H. E.) & MENON (K. P.). **The Stage of *Plasmodium gallinaceum* found in the Incubation Period—Second Observation.**—*Jl. Malaria Inst. of India.* 1941. Dec. Vol. 4. No. 2. pp. 179–180.

By the examination of the brain of fowls inoculated with sporozoites of *Plasmodium gallinaceum* from *Aëdes aegypti* at varying intervals it has been demonstrated that typical exoerythrocytic forms can be found as early as the fifth day. These are few in number and require prolonged search for their discovery. It is concluded that these are the forms developed from sporozoites and that they give rise later to the erythrocytic pigmented forms. The authors say that it is probable that a longer search will reveal the exoerythrocytic schizonts earlier even than the fifth day. *C. M. Wenyon.*

ADLER (S.) & TCHERNOMORETZ (I.). **Continued Passage of Extra-Erythrocytic Forms of *Plasmodium gallinaceum* in the Absence of Erythrocytic Schizogony.**—*Ann. Trop. Med. & Parasit.* 1941. Dec. 31. Vol. 35. No. 2. pp. 241–246.

The authors have shown that administration of quinine hydrochloride in daily doses of 150 mgm. per kilo of body weight will eliminate the pigmented erythrocytic forms of *P. gallinaceum* from the blood of fowls while leaving the exoerythrocytic schizonts intact. If brain emulsion of such a treated fowl containing exoerythrocytic schizonts is inoculated to a clean fowl which shortly after is placed on the above daily dosage of quinine, the development of exoerythrocytic schizonts takes place. Some of the merozoites produced by these schizonts enter the erythrocytes but they do not develop as far as the pigmented stage

before they are eliminated by the quinine. Such a fowl examined post mortem is found to have many erythrocytic schizonts in the brain but no malarial pigment in the organs. Five passages of the kind have been made, showing that exoerythrocytic development may occur in a number of passages without the development of any pigmented stages. In one fowl so treated cessation of quinine for one day was sufficient to allow the non-pigmented erythrocytic forms to reach the pigmented stage. *C. M. Wenyon.*

LAIRD (Raymond L.). **Observations on Mosquito Transmission of** *Plasmodium lophurae.*—*Amer. Jl. Hyg.* 1941. Nov. Vol. 34. No. 3. Sect. C. pp. 163–167.

BLACKWATER FEVER.

YUILE (Charles L.). **Hemoglobinuria.**—*Physiol. Rev.* 1942. Jan. Vol. 22. No. 1. pp. 19–31. With 1 fig. [47 refs.]

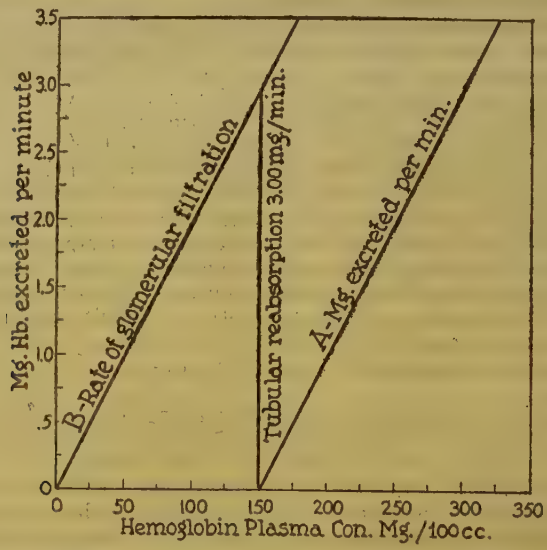
This review, which is a critical survey of the experimental findings relating to haemoglobinuria, is an attempt to reach a clearer understanding of the factors underlying the elimination of haemoglobin by the kidney.

The finding of granules of haemoglobin or its iron-containing breakdown products in the epithelium of the convoluted tubules following the injection of haemoglobin indicates that this portion of the kidney plays some part in the process of haemoglobin elimination, and for years a controversy has existed whether the tubular activity is one of excretion or reabsorption. A review of experimental work affords no positive evidence of tubular excretion and it would appear that, in most instances, an interpretation of the findings in favour of reabsorption could equally well be made. Evidence derived from the study of lower vertebrates also supports this view. Much of the early confusion was doubtless due to the fact that haemoglobin is readily observed in the capsules at the height of haemoglobinuria but is not demonstrable at later stages owing to the increased dilution. Furthermore, haemoglobinuria occurs in dogs in the presence of severe tubular damage caused by mercury poisoning, and in human beings, the rate of excretion has been found to be markedly elevated in cases of known glomerular damage.

Although it is now generally agreed that haemoglobin escapes through the glomerulus there is little agreement regarding the way in which it does so. Because serum albumen, the molecular weight of which is approximately the same as that of haemoglobin (68,800), does not normally appear in the urine, it has been suggested that haemoglobin escapes through the glomerulus only as the result of an induced transient injury. Careful evaluation of all the evidence available indicates, however, that glomerular injury is not the fundamental mechanism of haemoglobin excretion, and numerous studies have shown that intravenous injection of stroma-free haemoglobin solution has practically no pharmacological activity and produces no evidence of glomerular damage.

The modern filtration theory of renal function considers the glomerulus as a purely mechanical sieve containing innumerable pores each large enough to permit the passage of an inulin molecule (mol. wt. 15,000). Such a concept indicates only a minimum but not a maximum pore size. The upper limit may be set at a molecular size approximately that of haemoglobin. Muscle haemoglobin (mol. wt. 17,500) is excreted rapidly and has a clearance ratio with creatinine of about 0·58 in the dog ; and since there is some evidence of tubular absorption of this substance, its filtration rate has been estimated as about 0·75 times that of creatine. Haemoglobin has an estimated filtration ratio with creatinine of only about 0·03. This reflects the very low rate of haemoglobin excretion in relation to its concentration in the plasma, and suggests that under maximal conditions only about 3 per cent. of the pores in the membrane are large enough to allow a haemoglobin molecule to pass.

The author next passes to a consideration of the renal threshold for haemoglobin. He points out that the concept of a " glomerular threshold " was based largely on the ability to lower the initial threshold by about 46 per cent. to a fairly constant level by repeated diminishing daily injections, and the failure to find deposits of iron-staining material in the epithelium of the convoluted tubules following repeated sub-threshold doses. The lowered threshold was explained by assuming that the tubular epithelial cells became filled to such an extent that they would reabsorb no more. More recently it has been found that the renal threshold for haemoglobin in relation to plasma concentration may be lowered by 60 per cent. or more, depending on the size and number of



Graph illustrating the type of analysis of experimental data used to estimate tubular reabsorption. Line *A* represents the actually determined rate of renal hemoglobin excretion above the threshold. The parallel line *B* equals the rate of glomerular filtration if tubular reabsorption, the perpendicular distance between the two lines, reaches a maximum at the threshold and remains constant at higher levels.
[Reproduced from *Physiological Reviews.*]

daily injections sufficient to cause gross haemoglobinuria. Since after lowering the threshold to various levels the excretion rate curves are parallel to those obtained initially, and since under these conditions the estimated tubular reabsorption rate is lowered proportionally, it is not unreasonable to suppose that a complete cessation of tubular reabsorption would entirely eliminate the threshold. The constant level attained with diminishing daily doses in the earlier experiments suggests a state of equilibrium between the amount of haemoglobin reabsorbed by, and the amount of haemoglobin products removed from, the tubular epithelium daily, rather than a complete cessation of reabsorption. If modification of tubular reabsorption accounts for the lower threshold, the amount removed daily must be quite significant, because when the injections of haemoglobin are discontinued it returns to its initial level within a period of several weeks. Such a mechanism would also explain the absence of iron-staining pigment in the kidney after repeated sub-threshold injections because the amount picked up would be less than the rate of daily removal from the tubular epithelium.

The accompanying figure illustrates the type of graphical analysis of experimental data by which quantitative estimates of the glomerular filtration and tubular reabsorption rates of haemoglobin have been made. An average value for the initial rate of tubular reabsorption lies between 2·0 and 3·0 mgm. per minute, and values of less than 1·0 mgm. per minute have been obtained after lowering the threshold by about 70 per cent.

Bogniard and Whipple (1932) have shown that at least some of the iron-containing portions of haemoglobin are stored in the tubular epithelium, and more recently iron retention by the kidneys has been determined after the injection of haemoglobin containing radioactive iron. Single large injections were given to normal dogs and also to those in which the threshold had been markedly lowered by repeated injections. Tubular reabsorption values were estimated from the rate of pick up obtained by the graphical analysis just described, and the time required for the disappearance of haemoglobinaemia. The animals were subjected to viviperfusion 24 hours later, and comparisons were made between the estimates and the actual amounts of radioactive iron found in the kidneys. Calculated values ranged from somewhat over 40 per cent. of the injected amount in the normal group to about 20 per cent. in the group with the lowered thresholds. However, only about 16 per cent. of the injected iron was present in the kidneys of the normal animals contrasted with over 20 per cent. in the kidneys of comparable animals with lowered thresholds. It must be assumed that in normal animals there is a very rapid removal of haemoglobin after it is picked up by the renal epithelium ; and it must also be assumed that both the intake and output of haemoglobin by these cells are greatly diminished after repeated daily injections. If the low radioactive iron content of the kidneys in the normal animals represents the total amount reabsorbed during the period of haemoglobinaemia, it seems necessary to assume that the glomerulus is responsible, at least in part, for the threshold phenomenon, and that it is the permeability of this structure rather than the reabsorption by the tubular epithelium which is modified by repeated injections. However, the author reaches the conclusion that much of the evidence available at the present time favours the theory that tubular reabsorption alone is responsible for the threshold phenomenon, and final proof must await the outcome of further investigations.

Comparisons of the renal threshold level for haemoglobin in man and various animals are often difficult to make. Recent estimations suggest that the threshold level in dogs lies between 80 and 150 mgm. of haemoglobin per 100 cc. of plasma, and for man at about 135 mgm. per 100 cc.

The author next passes to a discussion regarding the manner in which haemoglobin is picked up and stored by the epithelium of the convoluted tubules. He concludes by pointing out that the foregoing concepts of renal haemoglobin examination are largely based on quantitative studies in which the urine was rendered and kept alkaline. The paper ends with a brief discussion of the effect of the reaction of the urine. *W. Yorke.*

FAHR (Th.). Die Speicherungsnephrosen. [**Storage Nephroses.**]—*Klin. Woch.* 1941. Aug. 30. Vol. 20. No. 35. pp. 873–875.

The author defines the group of nephroses which he designates as storage nephroses (Speicherungsnephrosen) as those which exhibit a histological, but no further demonstrable, sign of substances which are excreted by the kidneys. Such substances may be fat, carbohydrates, uric acid, etc., when they are present in abnormal quantities in the blood, they may be various proteins, bile, etc., which are excreted because they are foreign to the blood, or they may be substances foreign to the body, such as dyes and drugs.

After considering the nephroses due to the excretion of fat, carbohydrates and uric acid, the author passes to the second group in which he refers to the excretion of Bence-Jones protein, cholaemic nephrosis and the storage of haemoglobin in haemoglobinaemic nephrosis. This is seen in very varied conditions such as burns, frost bite, blackwater fever, gas gangrene particularly in pregnancy, and in arsenuretted hydrogen poisoning.

Macroscopically, the kidneys are of a dirty brown sepia colour, but microscopically the localization of the haemoglobin varied greatly in different cases. Sometimes it is present in large amounts in the capsules and tubules, but is completely absent from the epithelial lining of the tubules. In other cases there is an enormous diffuse storage of haemoglobin in the epithelium, together with some in the lumen of the tubules, but none in the Bowman's capsules. From the standpoint of the filtration-absorption theory these varied appearances can be explained as different phases of the excretion process, the former representing the filtration phase and the latter the re-absorption phase.

This explanation, however, cannot be entirely adequate, as in man one sometimes comes across cases in which, notwithstanding day-long haemoglobinuria, there is no storage of haemoglobin in the epithelium, whilst in other cases evidence of storage in the epithelium appears almost immediately. A case reported by Vormann is quoted in which, after a burn, haemoglobinuria developed immediately; the patient died four hours later and sections of the kidneys showed distinct haemoglobin storage in the epithelium.

Fahr concludes that these different localizations of the haemoglobin are not the expression of two excretion phases but are the result of two different methods of excretion, depending on the concentration of the excreted material. The glomerulus and the tubules form a functional unit in which a division of work has occurred. In the glomerulus very diluted solutions are filtered, whilst in the tubules elimination takes place in concentrated form. *W. Yorke.*

RIMINGTON (Claude). **Haemoglobinometry.**—*Brit. Med. Jl.* 1942. Feb. 7. pp. 177–178.

There is a need for a rapid method for the determination of total blood pigment in samples of whole blood. The determination should include not only oxyhaemoglobin and reduced haemoglobin, but also the abnormal pigments methaemoglobin and sulphaemoglobin sometimes met with after the administration of sulphonamides, and CO-haemoglobin. The author has recently been using a method of total blood-pigment determination in which all the haem pigments are converted into pyridine-haemochromogen, and the intensity of absorption of the latter around 550 mμ is measured upon the Hilger-Nutting photometer. The results possess a high degree of accuracy, and have the added advantage that they may be referred to a pure crystalline chemical substance—haemin—by means of which the instrument is calibrated. The method is based upon the procedure described by ROETS (1940) in South Africa.

Rimington classifies the various methods available for the determination of haemoglobin and comments briefly upon them, drawing attention to their disadvantages, and then gives the description of his own method which is reproduced here :

" A 1 in 500 dilution of blood in decinormal sodium hydroxide is made, using a standard or calibrated pipette. This dilution may, of course, be made in two steps, if it is preferred, as in the worked example quoted below. After a few minutes at room temperature a convenient volume, such as 10 c.cm., is measured into a small flask and one-fifth of the volume of pyridine is added. Upon mixing by gentle rotation the conversion of the haem pigments into the alkaline parahaematin is completed within a few seconds ; hence there is no necessity to allow the original blood dilution to stand for 10, 20, or even 40 minutes before proceeding, or alternatively to heat in a boiling-water bath as is required when the alkaline-haematin method is used.

" A pinch of good-quality sodium hydrosulphite ($Na_2S_2O_4$) is now added to the mixture, and the contents of the flask are swirled gently until the solid has dissolved. The immediate colour change to pink denotes the conversion of the pigments into pyridine-haemochromogen. Without undue delay (to guard against reoxidation) the solution is transferred to a photo-electric colorimeter cell and the light absorption in the region 550 to 555 mμ is measured, using a suitable filter (*e.g.* Ilford spectrum filter No. 605—yellow-green). From the calibration factor, obtained by using known weights of pure haemin instead of blood and proceeding as above, the haemoglobin content of the blood is then calculated.

Molecular weight of haemin, $C_{34}H_{32}O_4N_4FeCl = 651{\cdot}4$.

Iron content of haemoglobin = 0·334%

∴ Molecular weight of haemoglobin = 66,890.

$$\frac{\text{Haemoglobin}}{\text{Haemin}} = \frac{66{,}890}{4 \times 651{\cdot}4} = 25{\cdot}66.$$

" Should it be contended that the error involved in calculating the molecular weight of haemoglobin from its iron content is undesirably large, the results might alternatively be expressed in terms of haemin or haematin. The extinction ε of pyridine-haemochromogen prepared from crystalline haemin and using a photo-electric absorptiometer with Ilford No. 605 filter and 1-cm. cell was found to be 0·108 at a concentration of 1 mg. per 100 c.cm.

" Should no photo-electric colorimeter be available, the concentration of the pyridine-haemochromogen solution may be determined by one of the alternative methods, such as colour comparison in a colorimeter with a standard prepared from haemin (standard solutions of haemin in alkali

should be kept in the dark) or dilution while viewing with a hand spectroscope until the intensity of the α absorption band matches that of a standard, as described by Roets (1940). This last method is certainly the most simple and rapid, although not quite so accurate as the use of a colorimeter. Pure haemin is easily prepared according to Gattermann (1937), but should be recrystallized as follows:

"5 grammes of haemin is dissolved in 15 c.cm. of pyridine, and 40 c.cm. of chloroform is added. The solution is passed through a No. 3 or No. 4 sintered-glass filter to remove any protein and is run into a mixture of 250 c.cm. acetic acid + 5 c.cm. saturated NaCl + 4 c.cm. concentrated HCl, which is maintained at water-bath temperature. After cooling to room temperature the crystals are filtered and washed successively with 50 per cent. acetic acid, water, alcohol, and ether, and then dried.

"I have used the pyridine-haemochromogen method with equal success for specimens of plasma and urine containing haemoglobin, myohaemoglobin, or mixtures of these with their derivatives. It is only necessary to adjust the initial dilution so that the concentration of pigment in the final solution falls within the comfortable range for measurement.

Example.—1 c.cm. of blood was diluted to 100 c.cm. with decinormal sodium hydroxide. To 1 c.cm. of this solution was added 3 c.cm. of the alkali, then 1 c.cm. of pyridine and, after mixing, a pinch of sodium hydrosulphite. In a 1-cm. cell the reading on the Hilger-Nutting photometer at 552 mμ was 0·573. The calibration for this instrument had been found to be 0·62. Hence:

Hb per c.cm of blood $= 0{\cdot}573 \times 0{\cdot}62 \times 500$
$= 177{\cdot}6$ mg. per c.cm.
i.e. 17·76%

"The same result was obtained whether the determination was completed within five minutes or after allowing the mixture with alkali to stand for one hour and that with pyridine for a further half an hour."

W. Yorke.

PRICE (C. H. G.). **Blackwater Fever.**—*Jl. Roy. Army Med. Corps.* 1942. Apr. Vol. 78. No. 4. pp. 196–198.

In September 1940, five French soldiers from French Equatorial Africa were landed from a ship that had been bombed and sunk. All suffered from the effects of immersion and exposure and four developed symptoms suggestive of malaria. In three of them *P. falciparum* was found in the blood and the patients recovered after appropriate treatment. The fourth patient on September 20th developed pyrexia with rigors and anuria, and blood examination revealed the presence of *P. falciparium.* The blood count showed the red cells to be 2,500,000 per cmm., and the haemoglobin 70 per cent. The patient became rapidly jaundiced and the following day his blood count had fallen to 2,050,000 per cmm. A blood transfusion was given without any clinical reaction. On September 23rd the red cell count was 1,600,000 per cmm., but no parasites were found. The small quantity of urine passed on that day contained acid haematin in large amounts. Alkalies had been given and these resulted in the change of the reaction of the urine to alkaline. The blood urea was found to be 400 mgm. per 100 cc. There was terminal suppression of urine and death occurred on September 24th.

A post-mortem examination was performed and the findings are given in some detail. There was nothing unusual in these findings and the conclusion is reached that the distension of the proximal portion of the nephron was due to blockage of the collecting tubules and papillary ducts.

W. Yorke.

BHATTACHARJEE (Jagadish C.). **Blackwater Fever in Darjeelingterai.**—*Indian Med. Gaz.* 1941. Dec. Vol. 76. No. 12. pp. 734–737.

During the five years 1935 to 1939, 20 cases of blackwater fever have come under the author's observation in Siliguri, a town situated about 300 feet above sea level in the Darjeeling district of Bengal. The locality is hyperendemic for malaria, the spleen index amongst children under 12 years of age varying between 60 and 70 per cent. The climate is hot and moist in summer and cold and dry in winter. The rainfall between June and October is heavy.

Tables show the incidence of cases month by month and also the age incidence. The author deals with such matters as the relation of the onset of blackwater to quinine, the history of previous attacks, clinical manifestations, and the result of examination of the blood for malaria parasites. Details are also given regarding the treatment administered. The paper contains nothing new. *W. Yorke.*

MASSIAS (Charles). L'hémoglobinurie palustre. (Etude biologique). [**Blackwater Fever.**]—*Rev. Méd. Française d'Extrême-Orient.* 1941. Mar.–Apr. Nos. 3–4. pp. 175–184.

Two cases of blackwater fever encountered by the author are described in great detail. This is followed by generalizations on the pathology and treatment of the disease. The paper contains nothing new and requires no special notice here. *W. Yorke.*

BOYLE (A. Kerr). **Blackwater Fever and Blood Transfusion.**—*Jl. Roy. Army Med. Corps.* 1942. Jan. Vol. 78. No. 1. pp. 44–45.

The author states that blood transfusion is not indicated in every case of blackwater fever, but its value is very great in the early stages of toxic polyuric and relapsing cases. Small transfusions of 300 to 450 cc. should be given and repeated as often as required. Citrated blood is better than whole blood, especially in the polyuric type in which the alkali reserve is often lowered. It is not possible in West Africa at the present time to found and maintain a blood depot; the blood must be given as soon as it is withdrawn. The only practicable scheme is to have a list of voluntary grouped donors, but routine grouping is not enough, there must be direct test of the compatibility of the bloods of donor and recipient, and the blood of the donor must be free from parasites and its cells not abnormally fragile. [It is not easy to see how freedom from malaria parasites can be ensured. Direct blood film examination may not be enough.] The author makes use of a 12 oz. medical flat bottle, in which is put 30 cc. of 3·8 per cent. sodium citrate. The bottle will hold 300 cc. of citrated blood, and is partly immersed in a hot water bath during the process of direct transfusion. *C. W.*

ROY (B. C.) **Vitex Therapy in Blackwater Fever.**—*Jl. Indian Med. Assoc.* 1941. Sept. Vol. 10. No. 12. pp. 475–482. With 2 charts. [23 refs.]

After giving a lengthy summary of blackwater fever, which contains nothing new, the author passes to the treatment of the disease with

Vitex peduncularis [this *Bulletin*, 1921, Vol. 17, p. 306 ; 1924, Vol. 21, p. 604 ; 1940, Vol. 37, p. 837]. Instructions are given regarding the method of preparation and the dosage, but no satisfactory evidence is produced that Vitex therapy is of the slightest use in blackwater fever.

W. Yorke.

TRYPANOSOMIASIS.

NASH (T. A. M.). **A Study of the Causes leading to the Seasonal Evacuation of a Tsetse Breeding-Ground.**—*Bull. Entom. Res.* 1942. Jan. Vol. 32. Pt. 4. pp. 327–340. With 3 figs. on 1 plate.

The author has shown previously that in Northern Nigeria *Glossina morsitans* and *G. tachinoides* annually shift their breeding-ground in March from the edge of a residual forest island to the centre—a distance of some 40 yards. This move is associated with an increase in mortality among the last puparia to be found. His object in this investigation was to discover what prompts the female to move just before pupal mortality increases. The movement is attributed to the negative reaction to light developed by the tsetse fly when exposed to an unduly high temperature [see this *Bulletin*, 1938, Vol. 35, p. 338]. The period of migration coincides with an abrupt increase in the number of hours with a shade temperature above 90°F. (32°C.), the temperature at which the negative reaction to light begins. Hungry flies may overcome this avoidance of the light and feed at the forest edge ; but the females in late pregnancy, which do not feed, remain in the forest centre where they are not exposed to so high a rate of evaporation. Detailed meteorological data given in this paper define the environments of adults and pupae in a locality very close to the hot dry limits of the range of these two species.

V. B. Wigglesworth.

SAUNDERS (G. F. T.). **Preliminary Report on the Treatment of Sleeping Sickness by 4 : 4′-Diamidino Diphenoxy Pentane.**—*Ann. Trop. Med. & Parasit.* 1941. Dec. 31. Vol. 35. No. 2. pp. 169–174.

Details are given of 14 cases of sleeping sickness in the Gold Coast which were treated by 4 : 4′-diamidino diphenoxy pentane. The author summarizes his results as follows :—

" 1. Details are given of fourteen cases of sleeping sickness treated with 4 : 4′-diamidino diphenoxy pentane. In all cases the peripheral blood was sterilized by four injections of the drug.

" 2. Seven out of ten central nervous system cases were possibly cured. Of these, one (case 3/II) was very advanced.

" 3. Up to 65 injections were given without ill result. All cases who were apparently cured, except case 3/II, were symptomless after, at most, 20 injections.

" 4. Early cases appear to be cured.

" 5. Untoward results are trivial."

W. Yorke.

DAUBNEY (R.) & HUDSON (J. R.). **The Action of Two Aromatic Diamidines on *Trypanosoma congolense* Infections in Cattle ; with a Note on Delayed Poisoning by 4 : 4′-Diamidino Diphenoxy Pentane.**—*Ann. Trop. Med. & Parasit.* 1941. Dec. 31. Vol. 35. No. 2. pp. 175–186.

This paper gives information regarding the experimental treatment of cattle infected with *T. congolense* by 4 : 4′-diamidino stilbene (stilbamidine) and 4 : 4′-diamidino diphenoxy pentane (pentamidine). Cattle were inoculated with a local strain of the parasite, which is maintained in rabbits. The strain is of relatively high virulence and kills young cattle in from three to five weeks.

An attempt was first made to obtain some idea of the maximum tolerated dose and its therapeutic effect, and consequently doses of 20 and 15 mgm. per kilo. were administered. In later experiments, the effect of two or three smaller doses was ascertained. It was found that neither drug produced a complete cure. In doses of 10 mgm. per kilo. upwards, pentamidine produced immediate poisoning. Delayed poisoning occurred with single doses of from 5 to 15 mgm. per kilo. and with repeated doses of from 5 mgm. per kilo. upwards. Cattle can be brought to the premunized state with either compound. The authors describe in some detail the delayed toxic effects of pentamidine, as seen by them in two healthy calves, which were treated with three inoculations of 5 mgm. per kilo. at 7-day intervals.

The animals remained in normal health for 24 days after the first infection. On the 25th day, both animals showed symptoms, the respirations being more rapid than usual, and in one of them the urine was noticeably yellow. On the 28th day, one of the animals was down and semi-comatose and had to be killed. The other animal was lying down most of the 29th and 30th days and took very little food ; when made to rise, he was unsteady on his legs. During the next six days he made a gradual recovery and at the time of writing, four months later, he appeared to be quite healthy but his growth had undoubtedly been stunted.

Post-mortem examination of the animal which died revealed oedema of the gastric mucous membrane with opaque plaques 2 to 3 mm. in diameter, and scattered haemorrhages. The liver was swollen, pale, and mottled with putty-coloured spots. The kidneys were darker than normal, and there was a slight pinkish staining of the visceral fat. Histologically, the most important change was an extremely advanced fatty degeneration of the liver. *W. Yorke.*

FULTON (J. D.) & YORKE (Warrington). **Studies in Chemotherapy. XXVII.—Further Observations on the Stability of Drug-Resistance in Trypanosomes.**—*Ann. Trop. Med. & Parasit.* 1941. Dec. 31. Vol. 35. No. 2. pp. 221–227.

In this paper the history of strains of *T. rhodesiense* made resistant to a considerable number of chemotherapeutic substances since 1929 is brought up-to-date. The authors summarize their work as follows :—

" 1. The atoxyl-fast strain has preserved its character unchanged for 12½ years, during which it has been passaged by blood inoculation through a series of over 1,500 mice.

" 2. Three Bayer-fast strains were prepared and maintained by mouse passage. The first lost some of its resistance during the first year and all trace of resistance within four years ; the second lost some of its resistance

during the first year, but retained a considerable degree of resistance after four years ; the third strain, which was prepared by enhancing the resistance of the second strain by further long continued exposure to the drug, maintained its resistance unimpaired during a period of three and a quarter years.

" 3. Two undecane diamidine-fast strains were prepared, one in mice and the other in rabbits. Both these strains had lost some of their resistance within a year, and all trace of resistance within three and a half years.

" 4. The synthalin-fast strain behaved exactly as the undecane diamidine-fast strains."

W. Yorke.

SAUNDERS (G.). **After-History of Trypanosomiasis Cases treated by Bayer 205.**—*Jl. Trop. Med. & Hyg.* 1942. Feb. 16. Vol. 45. No. 4. pp. 25–26.

" (1) Of thirty-six cases of Trypanosomiasis (*gambiense*), followed up for thirteen years or more, thirty-four of the thirty-five who had definite nervous involvement have died of sleeping sickness, and the one survivor has relapsed.

" (2) An early case followed up for thirteen years is apparently cured.

" (3) Even in advanced cases, Bayer 205 may produce remission of many years."

[See this *Bulletin*, 1928, Vol. 25, p. 795 ; 1929, Vol. 26, p. 708.]

HAWKING (Frank). **The Biological Standardisation of Suramin (Antrypol, Bayer 205).**—*Quarterly Jl. Pharm. & Pharmacol.* 1941. Oct.–Dec. Vol. 14. No. 4. pp. 337–346.

This paper is of a rather technical nature and must be consulted in the original by those interested. The following is the summary :—

" 1. Methods are described for the biological standardisation of the toxicity and therapeutic potency of suramin (antrypol, Bayer 205).

" 2. When the toxicity of suramin was tested by injecting it intravenously into mice, the LD50 was found to be 0·63 (0·61–0·65) mgm. per gm., and the slope of the log-dose : probit-response curve was $9{\cdot}9 \pm 0{\cdot}8$.

" 3. When the therapeutic potency of suramin was tested by injecting it intravenously into mice infected with *Trypanosoma equiperdum*, the response being taken as the proportion of mice free from trypanosomes on the 3rd day after treatment, the RD50 was found to be 0·43 (0·36–0·50) γ per gm., and the slope of the log-dose : probit-response curve was $18{\cdot}3 \pm 6{\cdot}0$.

" 4. Tests are described by which it can be ensured that the toxicity of a tested sample of suramin does not exceed that of a standard preparation by more than 20 per cent., and that its therapeutic potency does not fall short by more than 20 per cent.

" 5. Suramin is hygroscopic and in moist atmospheres it will absorb water up to 40 per cent. of the original dry weight. The British preparation (antrypol) is issued with a water content of 11–14 per cent. ; Bayer 205 (germanin) as issued in ampoules appears to be anhydrous. When corrections are made for the different water content, the toxicities and therapeutic potencies of the two products are indistinguishable."

For the assistance of those who may wish to test the toxicity or therapeutic activity of any sample of suramin (antrypol, Bayer 205) two of Hawking's tables relating respectively to the toxicity and therapeutic potency of suramin, sample A, are reproduced. Sample A

was a batch of antrypol, the moisture content of which was 13·8 per cent. No special steps were taken to prevent its taking up water, but it can be assumed that it contained 14 per cent. of water when the experiments were made. It should be noted that suramin is hygroscopic and that if left exposed to moisture it will absorb up to 40 per cent. of the original dry weight, giving the final product a content of 28 per cent. water.

TABLE I.

Toxicity of suramin, sample A, according to examinations made at Hampstead. The table shows the proportion of mice which died within three days of treatment with suramin.

Dose mgm/gm.	Experiments with 2·5 per cent. solution			Total 2·5 per cent. solution	Experiments with 4 per cent. solution					Total 4 per cent. solution
0·35	0/20	0/20	—	0/40	—	—	—	—	—	—
0·42	3/20	1/20	3/20	7/60	0/20	—	—	—	—	—
0·50	8/20	0/20	1/20	9/60	1/20	7/20	3/20	1/20	5/20	17/100
0·60	17/20	3/20	11/20	31/60	7/20	7/20	12/20	10/20	7/20	43/100
0·72	18/20	9/20	15/20	42/60	13/20	14/20	13/20	14/20	11/20	65/100
0·86	—	—	—	—	19/20	19/20	20/20	20/20	19/20	97/100
No. of experiments	1	2	3	—	4	5	6	7	8	—
Sex of mice	M	F	M		M	M	F	M	F	

TABLE III.

Therapeutic potency of suramin, sample A.
The table gives the proportion of mice which showed no trypanosomes in the blood on the third day after treatment.

Dose γ per gm.	Exp. 1	2	3	4	5	6	7	8	Total
0·52	9/10	10/10	8/10	7/10	8/10	8/10	9/10	11/11	70/81
0·43	—	—	6/10	5/9	8/9	3/10	4/10	8/11	34/59
0·39	0/10	9/10	—	—	—	—	—	—	9/20
0·36	—	—	0/10	3/10	1/10	0/9	1/10	1/11	6/60
0·30	0/10	1/10	0/10	—	—	—	—	—	1/30
0·24	0/10	0/10	0/10	—	—	—	—	—	0/30
Sex of mice	F	—	M	M	—	F	M	F	
Log. RD50	0·662	0·557	0·650	0·620	0·620	0·663	0·642	0·610	Mean 0·6280±0·0349
Slope *b* ...	27·4	16·3	19·8	6·4	19·2	19·0	16·0	22	Mean 18·3±6·0

$$y = 18{\cdot}3x - 6{\cdot}47.$$

W. Yorke.

MAZZA (Salvador). Estadística de la enfermedad de Chagas en primer período, comprobada por la M.E.P.R.A. hasta el 30 de Junio de 1940. [**Figures of Chagas's Disease confirmed by the M.E.P.R.A. up to June 30th, 1940.**]—*Prensa Méd. Argentina.* 1941. Dec. 17. Vol. 28. No. 51. 11 pp.

The number of cases of Chagas's disease has increased with considerable rapidity in recent years, owing, it is almost certain, to more careful examination revealing more sufferers rather than to actual increase in incidence. In 1937, SCOTT (*History of Tropical Medicine*, Vol. 1, p. 538) was able to collect only 241 cases. By the end of June 1938, 370 had been recorded, and in two more years another 260, making a total of 630. Of these 559 had been proved by direct blood examination, 30 by xenodiagnostic methods, 22 by inoculation, 10 by the Machado-Guerreiro reaction, six by biopsy of a gland, two by biopsy of the primary chagoma and one post-mortem. The distribution of cases by Provinces was :—

	To 1938	To 1940	Total
Mendoza	106	67	173
Chaco	67	80	147
Santa Fe	64	31	95
S. del Estero	34	12	46
La Ríoja	17	12	29
Catamarca	10	16	26
San Juan	8	17	25
Salta	14	7	21
Jujuy	17	3	20
Formosa	10	2	12
Tucumán	7	5	12
Córdoba	4	3	7
Corrientes	5	1	6
Neuquén	3	3	6
Entre Rios	3	—	3
San Luis	1	1	2
Total	370	260	630

H. H. S.

TALICE (R. V.), COSTA (R. S.) & MARRA (J. A.). Estudio clínico y epidemiológico de focos de enfermedad de Chagas en el Dpto. de San José. [**Clinical and Epidemiological Study of Chagas's Disease in San José Department of Uruguay.**]—*Arch. Uruguayos de Med. Cirug. y Especialidades.* 1941. May. Vol. 18. No. 5. pp. 396–438. [Bibliography.]

The authors give an account of their investigations carried out in 1939–40 as to prevalence of Chagas's disease in certain parts of the Department of San José. They give details of 49 cases in children between the ages of 4 months and 14 years. In the dwellings of these patients *Triatoma infestans* was abundant, and fully half of these insects examined were harbouring the trypanosome. The parents and even many of the children are well aware of the characters and habits of these insects. Of the 49 examined, four had trypanosomes in their

blood, seen in thick drop preparations or proved by xenodiagnosis; 24 of the remaining 45 presented clinical symptoms and the haematological findings of the disease. None was suffering from the disease in an acute form; all were up and about; common symptoms were loss of flesh, enlarged glands, dacryoadenitis, anaemia, tachycardia, monocytosis, symptoms for which no cause other than the trypanosome infection could be discovered. There is little or no doubt that cases are more numerous than the authors' findings would infer. The paper has an extensive bibliography of 59 references, 38 of which are to papers of which Dr. TALICE is the author or part-author. *H. H. S.*

MAZZA (Salvador) & JÖRG (Miguel E.). Anatomía patológica de casos mortales de enfermedad de Chagas. [**Pathology of Chagas's Disease.**] —*Prensa Méd. Argentina.* 1941. Nov. 12. Vol. 28. No. 46. 4 pp.

LEISHMANIASIS.

BRAHMACHARI (Upendra Nath). **A New Organic Antimonial for the Treatment of Kala-Azar by Intramuscular Injection—Neostebene.**—*Jl. Trop. Med. & Hyg.* 1941. Dec. 1. Vol. 44. No. 23. pp. 158–160.

The author, who introduced urea stibamine for the intravenous treatment of kala azar in India, has now brought forward another product, a derivative of p-amino-phenyl-stibinic acid with an antimony content of nearly 41 per cent., which can be administered intramuscularly. This new compound, given the name neostebene, has been administered in doses of 0·1 gm. twice a week, in a series of 10 cases, till a total of 1 to 4 gm. has been given. As far as it is possible to judge at present the treatment has been highly successful, but a further report is promised when sufficient data to allow of comparison with other forms of treatment have become available.

C. M. Wenyon.

PANDE (P. G.). **A Natural Case of Cutaneous Leishmaniasis in a Bullock in Assam.**—*Indian Jl. Vet. Sci. & Animal Husbandry.* 1941. June. Vol. 11. Pt. 2. pp. 98–104. With 4 plates. [24 refs.]

The case recorded is that of a bullock which was purchased from a wandering cattle dealer in Assam. At the time of purchase the animal had several nodular lesions on the hind legs extending from the hock to the fetlocks. The owner stated that other animals of the batch were observed to have similar lesions on the feet and tail. About two months after purchase the nodules became transformed into sores, in which condition they were first seen by the author. Examination of smears and sections of excised tissues revealed an infection with parasites which did not differ from *Leishmania donovani* or *L. tropica.* As oriental sore does not occur in Assam, while kala azar is of common occurrence there, the author favours the view that the parasite is *L. donovani* and that the case was one of kala azar, in which ulcerative lesions of the skin have been described. The author's diagnosis of a leishmanial infection was confirmed by workers at the Calcutta School of Tropical Medicine. *C. M. Wenyon.*

UNION OF SOVIET SOCIALIST REPUBLICS. REP. SCIENT. RES. WORK OF ALL-UNION INST. EXP. MED. [VIEM] FOR 1938–9. Moscow-Leningrad. 1940. pp. 108–109. [In Russian.]—[**Reservoir Hosts of Cutaneous Leishmaniasis.**]

During 1937–1939 parasitological expeditions, under the leadership of Prof. E. PAVLOVSKY, were engaged in a search for reservoir hosts of human cutaneous leishmaniasis and for breeding places of the sandfly vectors, in the endemic regions of Turkmenistan, Middle Asia.

In a summary of the results (mostly not yet published) it is stated that among the large numbers of local animals examined microscopically there were more than a thousand gerbils, *Rhombomys opimus*, which are the commonest representatives of the desert fauna. Up to 60 per cent. of these rodents proved to be naturally infected with cutaneous leishmaniasis. The identity of the gerbil and human parasites was established (1) by infection of the rodents with material from human sores (up to 100 per cent. positive results), and (2) by experimental transmission of the infection from gerbil to man. In addition to *R. opimus*, spontaneous infections were found in two other species of gerbils and in a marmot [all unnamed].

The examination of sandflies captured in the burrows revealed infections with the leptomonad forms of leishmania, which in some catches were present in up to 35 per cent. [The species of Phlebotomus is not named.]

It is concluded that cutaneous leishmaniasis is a typical zoonosis, the main sources of human infection, under desert conditions, being the burrows of gerbils. These conclusions have been confirmed in practice, for in one settlement, within a highly endemic area, the destruction of the rodents in their burrows (with chloropicrin) was followed by a decrease in the incidence of human infection from 70 to 0·4 per cent.

C. A. Hoare.

FEVERS OF THE TYPHUS GROUP AND OTHER FEVERS.

OTTO (R.) & BICKHARDT (R.). Ueber das Gift der Fleckfieberrickettsien. [**The Toxin of Typhus Rickettsiae.**]—*Ztschr. f. Hyg. u Infektionskr.* 1941. Dec. 27. Vol. 123. No. 4. pp. 447–462. With 2 figs. [19 refs.]

Emulsions of yolk-sac cultures of *Rickettsia mooseri* have already been shown by GILDENMEISTER and HAAGEN to be toxic. The authors have now shown that highly purified suspensions of Rickettsiae of the same kind and prepared from the same source also contain a toxin which is neutralized by specific immune sera of animals, convalescents and inoculated persons. A specific toxin has also been demonstrated in suspensions of *R. prowazeki* purified in the same way from yolk-sac cultures. The toxin was found in purified suspensions made from the lungs of mice inoculated by the intranasal route with *R. mooseri* and also with a strain of *R. prowazeki* which had acquired increased virulence for mice through a series of "lung passages" in these animals.

The quantity of the toxin was roughly proportional to the number of Rickettsiae contained in the suspensions, as estimated by observation

of stained films. It was an endotoxin because the Rickettsia-free fluid obtained from suspensions by filtration or centrifugation was found to be non-toxic, but it differed from the endotoxins of bacteria such as the Kruse-Shiga bacillus in being easily destroyed by heat and chemicals. Yolk-sac suspensions, for example, lost their toxicity in 16 hours at 37°C., and in 8 to 10 days at 4°C., but remained infective to guineapigs. The toxins were also destroyed by treatment with formol or phenol.

The action of the toxins on animals was quite different from that of infection caused by the virus; mice were killed by lethal doses of the toxin in three to eight hours, very exceptionally in periods up to 24 hours, whereas death from infection did not occur in less than three days. *John W. D. Megaw.*

BENGTSON (Ida A.) & TOPPING (Norman H.). **Complement-Fixation in Rickettsial Diseases.**—*Amer. Jl. Public Health.* 1942. Jan. Vol. 32. No. 1. pp. 48–58. With 3 figs. [19 refs.]

The experiments were in extension of those recently recorded by the same authors [see this *Bulletin*, 1942, Vol. 39, p. 146].

They were carried out with the special object of finding whether the complement-fixation test would be a satisfactory means of differentiating between endemic typhus and Rocky Mountain spotted fever. The Weil-Felix reaction does not help in this respect and the immunity test in guineapigs sometimes fails owing to secondary infections or the existence of non-specific immunity.

The antigens, as in the previous tests, were prepared from yolk-sac cultures of the virus of endemic typhus taken at the fifth or sixth passage. A control series of tests was made in persons suffering from the following diseases (the figures in brackets show the number of cases of each disease). Tuberculosis (14), leprosy (10), malaria (6), syphilis (10), rheumatic fever (10), undulant fever (7), tularaemia (13), typhoid fever (8), trachoma (8). In none of these cases did full fixation occur in titres higher than 1 in 4.

In two cases of laboratory infection with endemic typhus the test was made on several occasions with the following results.

Day of Disease	6th	10th	15th	85th	180th
Case 1—					
Complement fixation titre ...	?	1–8	1–4,096	1–1,024	1–512
Weil-Felix titre	1–80	1–1,280	1–40,960	1–320	1–160

Day of disease... ...	6th	7th	14th	90th
Case 2—				
Complement fixation...	1–2	1–4	1–8	1–512
Weil-Felix	1–320	1–2,560	1–5,120	1–640

The second case was regarded as exceptional because, in a series of 15 proved cases of endemic typhus, complement fixation titres ranging from 1–128 to 1–8,192 were found in every serum tested; a single sample was taken in each case and the period which had elapsed since

the onset of the fever varied from 9 days to 8 months; the highest titres were found in recent cases. In 38 cases diagnosed on clinical grounds the results were very much the same.

The fixation titres in 53 cases of former infection with endemic typhus are shown in the form of a graph whose trend can be gathered from the following average figures, some of which are based on a small number of cases.

Months after infection ...	2	6	15	36
Complement fixation ...	1–512	1–64	1–32	1–8
Weil-Felix	1–80	1–80	1–20	1–10

The complement-fixation titre rises later than that of the Weil-Felix reaction, but significant titres (1–8 and upwards) persist for long periods, whereas significant Weil-Felix titres of 1–160 are rarely seen after six months.

Similar tests were made in 20 active and 10 old cases of Rocky Mountain spotted fever. All of the old cases (8 months to 2 years) gave completely negative responses. Of the 20 recent cases 14 were completely negative and only one of the others reacted completely in dilutions higher than 1–2. The exceptional case reacted on the 14th day up to a titre of 1–256; this person had lived in a place where endemic typhus occurred and so may possibly have had a previous attack, or there may have been a relationship with the high Weil-Felix titre which was 1–20,480 on the same day.

The complement-fixation test is therefore regarded as being of considerable value in differentiating between endemic typhus and Rocky Mountain spotted fever: it may be positive up to five years or more after the illness.

The results of the Weil-Felix test in the cases of spotted fever are interesting; they showed very great variations. In one case the reaction was completely negative on the 7th day; the titre was only 1–20 in three cases tested on the 14th, 18th and 21st days respectively. On the other hand it was 1–5,120 in one case on the 14th day and 1–20,480 in another case on the 14th day. In the cases of endemic typhus the results were far more consistent: a titre of 1–1,280 or over was reached in every one of the 11 proved cases in which the test was made between the 9th and 35th days. In four old cases tested from 74 to 250 days after the onset the titre ranged from 1–40 to 1–1,280.

In the clinical differential diagnosis importance is attached to the rash which usually appears first on the body in endemic typhus and first on the extremities in spotted fever. *John W. D. Megaw.*

ROMERO ESCACENA (G.), BOLINCHES (J.) & ALVAREZ (M.). Estudio clínico y experimental del tifus exantemático.—Epidemia de Sevilla. (Segunda communicación. [**Clinical and Experimental Study of Exanthematic Typhus—Seville Epidemic. (Second Communication.)**]—*Rev. Clin. Española.* 1941. Aug. 1. Vol. 3. No. 2. pp. 106–115. With 7 figs. [48 refs.]

[For an account of the first communication, see this *Bulletin*, 1942, Vol. 39, p. 139.]

Five strains of virus were isolated by guineapig inoculation from persons suffering from louse-borne typhus fever. The blood was

taken between the 3rd and 18th days. Four of the strains caused scrotal reactions in guineapigs within 5 to 8 days. Passages of the virus were made chiefly through guineapigs and rats. Mice which were inoculated had inapparent attacks, but their blood was infective to guineapigs.

Full details are given of the experiments; the results can be summarized as follows:—The virus corresponds to the murine strain in (1) the incubation period, which was less than five days in some of the animals; (2) the orchitic reaction in inoculated guineapigs; (3) febrile relapses which were frequent, and (4) the obvious febrile reactions in the rats. On the other hand it corresponds to the historic virus in (1) the incubation period, which was more than six days in the majority of the animals; (2) orchitic reaction, seen only occasionally in the later passages of the virus; (3) complete absence of orchitis in one of the five strains, and (4) the mortality in rats, which was very low.

The conclusion is reached that the strains are not really murine, and that the responses observed in experimental animals are not decisive criteria on which to base the classification of the virus; they represent merely the results of the adaptation of the virus to new kinds of animal reservoirs of infection.

One cross-immunity test gave an interesting result. A rat which had shown a slight orchitic reaction after inoculation gave a definite febrile reaction to further inoculation of the same virus four months later, though the attack was much less severe.

John W. D. Megaw.

MRUGOWSKY (J.). Typischer und atypischer Krankheitsverlauf beim Fleckfieber. [**Typical and Atypical Cases of Typhus Fever.**]—*Med. Klin.* 1942. Feb. 27 & Mar. 6. Vol. 38. Nos. 9 & 10. pp. 193–197; 221–223. With 3 figs.

The author had recently investigated more than 100 cases of typhus fever in various countries of Middle Europe; he remarks early in the paper that "the more one sees of typhus fever, the more varied is the clinical picture."

The patients often thought that they had influenza and consulted the doctor only when they became seriously ill; this condition was reached in most of the cases by the third or fourth day. The chief features of 28 patients seen before the appearance of the rash were:—16 had pain in the muscles, usually of the calf; 14 had a palpable spleen; 13 had conjunctival injection; 13 had a feeble pulse; 12 had bronchitis; 6 had swelling of the feet; 5 had mental confusion.

The symptoms often suggested some other disease, such as influenza, acute pharyngitis, appendicitis, polyarthritis or nephritis.

Special attention is called to the occurrence of a pronounced remission or intermission of the fever which was often seen from the fourth to the seventh day and lasted a few hours. The rash was sometimes seen as early as the first to the third day, especially in severe cases; in two patients it was first seen on the tenth day, and in one as late as the twelfth day. The systolic blood-pressure was 90 mm. or less. In several cases death occurred within two to four days of the onset; in these cases the rash was petechial from the outset.

One remarkable case is recorded in which there was no fever till the 16th day, on which the patient died.

The author states that no death from typhus has ever been reported in a patient who had been fully immunized by Weigl's method, but he does not regard other methods, such as that of Otto and Wohlrab, as being so reliable. *John W. D. Megaw.*

LUZ (Karl). Ueber sporadisches Fleckfieber. [**Sporadic Typhus Fever.**]—*Muench. Med. Woch.* 1942. Mar. 6. Vol. 89. No. 10. pp. 207–209.

A description is given of the features of 41 cases of the disease seen in Leipzig: 36 of the patients were Poles, the rest were Germans.

About one-third of the patients had catarrhal or follicular pharyngitis at the onset; in two cases appendicitis was simulated. In mild cases the rash was usually slight or fleeting, and in 16 cases no rash could be seen. Eleven of the cases were classed as ambulatory, in none of these was a rash seen; 20 were classed as severe, all but two of these had a rash. There were three deaths, only one of which occurred in the 36 Polish patients, whereas two of the five Germans died.

Two of the cases in Germans were ambulatory although the patients had never previously been exposed to the risk of infection and so could not have acquired immunity against the disease. All the patients gave positive Weil-Felix reactions in titres of 1–100 and over on the sixth day. *John W. D. Megaw.*

WALTHER (G.). Nachkrankheiten in der Fleckfieber-Rekonvaleszenz. [**Sequelae during Convalescence from Typhus.**]—*Klin. Woch.* 1942. Mar. 21. Vol. 21. No. 12. p. 269.

Reference is made to recurrence of slight fever during convalescence, two to three weeks after the subsidence of the original attack, and to a form of oedema resembling urticaria or Quincke's oedema. The temperature may rise to 37·8°C. or exceptionally to 39°C., with headache, rapid pulse and malaise. After a day or two, convalescence is resumed. The author attributes these conditions, and similar conditions in other infective diseases, to the development of an allergic state and holds that the agglutinins and protective substances in typhus show a great increase after the disease has subsided, to be reduced again after about one month.

In one case fully described there was no evidence of relapsing fever to account for the febrile sequela, and trench fever was ruled out. This patient had polyneuritis together with urticaria after a typical attack of typhus. *C. W.*

PATIÑO-CAMARGO (Luis). Brote epidemico de tifo negro o exantematico en Bogota. [**An Outbreak of Black or Exanthematic Typhus in Bogota.**]—*Rev. Facul. de Med.* Bogota. 1941. Dec. Vol. 10. No. 6. pp. 425–441. With 10 figs. on 4 plates.

Bogota, in Colombia, lies near the equator at a height of about 8,500 feet. Twenty cases, of which three were fatal, are reported as having been treated in the hospitals of the town during July and August, 1941. The Weil-Felix reactions against *Proteus OX19* were strongly positive in all and the virus, isolated from two patients and from lice collected from two patients, was identified as *Rickettsia prowazeki*.

An interesting reference is made to the occurrence of a devastating epidemic in the same area in 1630 : the name *tabardillo* (burning fever) was applied to this outbreak. *John W. D. Megaw.*

DURAND (Paul) & BALOZET (Lucien). Préparation d'un sérum anti-exanthématique par inoculations de rickettsias de poumons de souris. [**Anti-Typhus Serum Prepared by Inoculation with Mouse-Lung Rickettsiae.**]—*Arch. Inst. Pasteur de Tunis.* 1940. Dec. Vol. 29. No. 4. pp. 363–388. With 1 fig. [14 refs.]

Suspensions made from the lung of a mouse inoculated by the respiratory route contain as many minimal infecting doses as 10,000,000 to 200,000,000 infected guineapig brains. Stated in other terms a mouse-lung weighing less than half a gramme has the same virulence as fifty to a thousand tons of guineapig brains.

Suspensions of living Rickettsiae prepared from the lungs of mice heavily infected with *Rickettsia prowazeki* or *R. mooseri*, after suitable treatment, were injected subcutaneously or intravenously into horses and asses.

The protective powers of sera prepared in this way were found to be much greater than those of convalescent sera, judging by the results of the intradermal test, in which serum and infective agent are mixed before injection. The Weil-Felix titres of the sera did not correspond to the responses to the intradermal tests.

The curative value of the sera can only be judged by therapeutic tests on human patients.

Details are given of the technique employed and of the findings ; these will be found very useful to workers who wish to investigate the possibilities of preparing a curative serum. *John W. D. Megaw.*

SPARROW (H.) & MARESCHAL (P.). Sensibilité de l'organisme humain vis-à-vis des rickettsias de typhus murin I de Tunis. [**The Sensitiveness of the Human Body to the Tunis I Strain of Murine-Typhus Rickettsiae.**]—*Arch. Inst. Pasteur de Tunis.* 1940. Sept. Vol. 29. No. 2 & 3. pp. 238–249. With 1 chart.

The authors begin by emphasizing the need for a thorough investigation of the properties and stability of any living virus before it is taken into use for the protective inoculation of human beings. With murine typhus, laboratory infections are difficult to avoid, but these yield information about the safety of extending the experiments to human beings. Human subjects of experiments must be young persons who are in good health and are under constant medical supervision. Care must be taken to ensure the purity of the strain which is used, especially in the case of a laboratory situated in an endemic locality.

The experiments now reported were made on young persons suffering from diseases for which treatment by pyretotherapy is useful. The vaccine was a suspension of living murine Rickettsiae obtained from the intestines of lice inoculated by Weigl's method. The doses are expressed in terms of the amount of virus contained in the intestine of one infected louse. Inoculation was by the subcutaneous route.

The largest dose, one louse intestine, was given to each of five persons. In four cases there was a sharp local reaction at the site of the inoculation about the third day and febrile attacks started between the seventh and ninth days ; they lasted from six to ten days. The

reactions to *Proteus OX19* reached their highest titres (1–800 to 1–120,000) from the 10th to the 20th day. A rash was seen in only one case ; it appeared on the sixth day and extended over the trunk and limbs. Three of the subjects were later found to be immune, the fourth was not tested. In the fifth case there was no reaction except that the Weil-Felix titre which had been 1–240 before inoculation rose to 1–32,000 after about a month. [This result suggests the possibility of immunity resulting from a previous attack of murine typhus.]

One patient was given a dose of 1/10 of a louse intestine ; he had an attack of fever lasting 11 days and a generalized rash which appeared on the fourth day. The Weil-Felix titre was 1–12,000 on the 19th day.

Two persons were given 1/100 of a louse intestine ; both had inapparent attacks ; in one case the Weil-Felix titre was 1–800 and in the other 1–24,000. Complete immunity was found in the one case in which the test was made.

Two persons were given 1/1,000 of a louse intestine ; another 1/100,000, and another 1/1,000,000. In these four cases there was no response of any kind and no immunity resulted from the inoculations.

Inoculation by instillation of the virus into the conjunctiva was tried in six persons. Five of these received doses of 1/100 of an intestine or less and no response followed ; all were later found to be susceptible. The sixth person was given a dose of one louse intestine ; after 17 days' incubation he developed a mild attack of fever lasting six days ; no rash was seen. The Weil-Felix titre reached 1–6,400 on the 28th day after inoculation and immunity was established. The seventh patient was given 1/30 of an intestine : he had no reaction except that the Weil-Felix reaction was positive, 1–1,600 on the 34th day after inoculation. His immunity could not be tested.

Among the conclusions reached were—(1) Conjunctival instillations cause milder attacks with longer incubation periods than similar doses by the subcutaneous route. (2) Lice could not be infected by feeding on persons inoculated by the above methods. (3) Full immunity is established in cases in which the dose is sufficient to cause a positive Weil-Felix reaction, even if the attack is inapparent. Immunity is not produced unless actual infection has been caused. (4) The severity of the attack is greater when large infecting doses are given than when the doses are only just enough to cause infection. (5) Individual differences in susceptibility occur, and (6) Rats are more susceptible to murine virus than man ; this conclusion is qualified by the proviso that it has only been proved to hold in the case of the virus " murine I " and of persons living in an endemic area.

John W. D. Megaw.

SPARROW (Hélène). Abondance des rickettsias du typhus murin cultivées dans les poux. [**The Richness in Rickettsia Bodies of Cultures of Murine Typhus grown in Lice.**]—*Arch. Inst. Pasteur de Tunis.* 1940. Sept. Vol. 29. No. 2 & 3. pp. 250–261. With 1 chart.

Suspensions of the " murine virus 1 of Tunis " were made from the intestines of lice infected by Weigl's method. The virus had already undergone 275 passages through rats and had maintained a remarkable degree of constancy in its virulence for animals and human beings.

Varying doses of the living virus were injected by the subcutaneous route into 63 rats and 22 guineapigs. The extraordinary extent to which the murine Rickettsiae multiply in the intestine of the louse is shown by the fact that doses as small as 1/1,000,000,000,000 of an infected intestine caused infection in rats. This is comparable with the multiplication that takes place in lice infected with the historic virus; it suggests that the louse intestine at the highest degree of infection must contain something like a billion (English nomenclature) Rickettsiae, and also that the ordinary methods of counting Rickettsiae give far too small results.

A suspension made from the brain of an infected rat contains only about 100,000 infecting doses for rats.

With very small infecting doses the febrile attacks in rats are much less severe than with large doses; death never occurs, yet the animals become solidly immune to both murine and historic virus even in cases in which the Weil-Felix reaction remains negative and in cases which show no febrile reaction.

In guineapigs similar results were obtained; fever and orchitis were produced in one animal which had been given a dose of 1/10,000,000,000 of an intestine. Immunity against historic virus was produced in another animal by a dose of 1/100,000,000,000 of an intestine.

John W. D. Megaw.

DE MAGALHÃES (Octavio) & MOREIRA (João Affonso). Typho exanthematico em Minas Geraes. Aspectos clinicos. [**Exanthematic Typhus (Tick-borne) in Minas Geraes.**]—*Brasil-Medico.* 1940. Mar. 30. Vol. 54. No. 13. pp. 195–202. With 13 figs.

[This is the first part of an article of which the second part was reviewed in this *Bulletin*, 1941, Vol. 38, p. 443.]

The principal vector is believed to be *Amblyomma cajennense*; the disease is chiefly rural, it shows a great variety of manifestations and the mortality is not so high as has been suggested by previous records which have dealt chiefly with very severe cases.

Ambulatory forms with very trifling manifestations probably account for the immunity of large numbers of persons in the affected areas. The occurrence of very mild cases has been proved by the isolation of Rickettsiae from the blood in such cases. In permanent foci of the disease there may be long periods of "silence" followed by outbreaks in which attacks occur even in persons who have lived a long time in the affected localities.

The mildest forms of the disease are likely to escape notice; the only symptoms may be those of coryza or bronchitis, there is no enlargement of the liver or spleen. In cases of average severity there is headache and loss of appetite for a day or two, followed by high fever with chills, prostration, injection of the conjunctivae, vomiting and irritability. The rash appears within two or three days, usually first on the shoulders; it may be difficult to detect or may be intense and generalized, affecting the face, scalp, palms and soles as well as the rest of the body. The mind is clear, the urine has a trace of albumen. Low temperatures may occur, but these are also sometimes seen in the most severe cases.

The grave form is the one that has been most often described. The onset is usually sudden with severe pains, vomiting, high or low fever, great prostration and sometimes delirium. Differential diagnosis is impossible at first, but the early onset of severe nervous manifestations

is suggestive; these may assume a great variety of forms. The swollen face and injected conjunctivae are also conspicuous features. Among 105 proved cases no rash could be detected in 11 per cent. The day of appearance of the rash was as follows in 101 cases: 2nd, 5; 3rd, 10; 4th, 20; 5th or 6th, 40; 7th, 4; 8th to 10th, 2; doubtful, 8; no rash seen, 12. Persistent staining after petechial eruptions may be seen up to two months after the attack. The clinical signs and symptoms are given in detail; they correspond to a striking degree with those seen in Rocky Mountain spotted fever.

John W. D. Megaw.

DURAND (Paul), GIROUD (Paul) & SPARROW (Hélène). Inoculation pulmonaire du virus pourpré (fièvre des Montagnes Rocheuses). [**Pulmonary Inoculation of the Virus of Rocky Mountain Spotted Fever.**]—*Arch. Inst. Pasteur de Tunis.* 1940. Sept. Vol. 29. No. 2 & 3. pp. 228–233. With 1 fig.

Durand and Sparrow have already described the results of the pulmonary inoculation of certain rodents with the viruses of historic and murine typhus and of boutonneuse fever. [See this *Bulletin*, 1940, Vol. 37, pp. 572, 849.] The experiments now recorded were made with three strains of the Rocky Mountain virus obtained from R. R. Parker. One strain was highly virulent, another was of moderate virulence and the third was of consistently low virulence, it caused no scrotal reaction and was rarely fatal to inoculated animals.

The results varied according to the virulence of the Rickettsiae. In the case of the highly virulent strain mice and rabbits reacted in the same way as to the Rickettsiae of murine typhus and boutonneuse fever, by pulmonary consolidation with the production of abundant Rickettsiae after intratracheal inoculation of suspensions made from tissues of infected guineapigs. With the strain of moderate virulence the results were analogous to those obtained when using the historic virus: this correspondence was shown by the necessity for adopting the preliminary measure of subjecting the invertebrate host to a procedure for the reactivation of the virus. The method adopted was to allow the infected ticks to feed for two days on a guineapig and then keep them for four days at a temperature of 33°C. After repeated passages through the lungs of mice this strain was found to retain its property of moderate virulence as shown by guineapig inoculation tests.

The strain of low virulence killed only four out of fifteen inoculated mice; in two there was some degree of consolidation of the lung but no Rickettsiae could be found.

[This paper is a fuller account of the work previously reported and abstracted in this *Bulletin*, 1940, Vol. 37, p. 849.]

John W. D. Megaw.

DURAND (Paul) & GIROUD (Paul). Essais de vaccination contre le virus pourpré (fièvre des Montagnes Rocheuses) au moyen de rickettsias tuées par le formol (souches pulmonaires). [**Experiments in Vaccination against the Virus of Rocky Mountain Spotted Fever by Rickettsiae obtained from Lung Cultures and killed by Formol.**]—*Arch. Inst. Pasteur de Tunis.* 1940. Sept. Vol. 29. No. 2 & 3. pp. 234–237. With 1 fig.

The results of the experiments by the authors on vaccination against historic typhus by Rickettsiae killed with formol suggested the present

experiments in which they used a vaccine prepared with the Rickettsiae of Rocky Mountain spotted fever obtained from the lungs of infected mice.

Suspensions of the Rickettsiae in human or horse serum were used and a high degree of protection was demonstrated in inoculated guineapigs. Three Cynocephalus monkeys and six guineapigs were given suitable doses of the suspension by the intradermal route; 25 days later all the animals were found to be protected against doses of infective material which caused the death of the control monkey in 11 days after 6 days of fever, and the usual reactions in the guineapigs.

The vaccines caused neither local nor general reactions.

John W. D. Megaw.

WOHLRAB (R.). [**Immunizations against Typhus.**]—*Med. Klin.* 1941. May 23. Vol. 37. p. 532. [Summary prepared for *War Medicine.* Chicago.]

Wohlrab reviews attempts at preparation of effective vaccines against typhus, pointing out that experiments with living vaccines did not produce practical results. The first vaccines prepared with killed rickettsias likewise were not sufficiently effective, but Weigl produced an effective vaccine by infecting lice by means of anal clysters. This method enabled him to infect lice in the absence of typhus patients. After the lice have been infected, they are fed for eight to ten days on persons convalescing from typhus. Then the vaccine is prepared from the stomachs of the lice. This vaccine is injected three times in five days. It proved its value in Poland, in China and in Ethiopia. The protection it confers persists for one to two years. Since the preparation of this louse vaccine is somewhat complicated, search was made for simpler methods for the multiplication of rickettsias. Cox's method of utilizing the vitelline sac of the chicken embryo proved most satisfactory and was used by Otto for the mass production of *Rickettsia prowazeki.* . The former method of killing by heating to 60°C. has now been abandoned because it impairs the antigen. Immunization is done by injecting the vaccine three times (0·5 cc. once and 1 cc. twice) at five day intervals. It was proved on guineapigs that the vaccine obtained by the chicken embryo method has practically the same degree of efficacy as has the louse vaccine of Weigl. However, in eggs the growth of rickettsiae is not always uniform, and so it is necessary to continue Weigl's method as well. It may become possible to improve the quality of the vaccines after further research on the immunizing constituents of rickettsias that go into solution (perhaps toxins). Protective effects could be obtained with extracts from egg yolk and cell culture, filtrates that were practically free from rickettsias. Experiments have been made also with a vaccine of Rickettsia mooseri, but the heterologous immunity produced by it is, of course, somewhat inferior. Discussing attempts at passive immunization, the author states that the production of immune serum in horses has been satisfactory only with R. mooseri. The use of pooled convalescent serum was tried last year in Poland but proved ineffective.

[For details of the preparation of the Cox vaccine, see this *Bulletin*, 1942, Vol. 39, p. 381.—*Ed.*]

HETSCH (H.). Die Schutzimpfung gegen Flecktyphus und die zu ihr verwendeten Impfstoffe. [**Protective Inoculation against Typhus Fever and the Vaccines Employed.**]—*Med. Klin.* 1942. Apr. 10. Vol. 38. No. 15. pp. 341–342.

This is an exceptionally clear and concise account of the more important methods of protective inoculation against typhus fever. The vaccines discussed have already been described in this *Bulletin* and there is no indication that German workers have yet discovered any new weapon in the war against typhus.

The author considers that Weigl's vaccine is the only one that has been proved to be successful on a large scale in human beings, but he states that Cox's yolk-sac vaccine is equally effective in producing immunity in animals. He holds that a final judgment on the latter and other vaccines must await human experiment on a large scale.

John W. D. Megaw.

LILLIE (R. D.). **Pathologic Histology in Guinea Pigs following Intraperitoneal Inoculation with the Virus of "Q" Fever.**—*Public Health Rep.* 1942. Feb. 27. Vol. 57. No. 9. pp. 296–306. With 1 plate.

Three strains of the virus, including the original *Rickettsia burneti* were used ; the tissue reactions to all three were essentially similar.

Altogether 76 guineapigs were employed ; the examinations were made at intervals ranging from one to twenty-five days after inoculation. Full details are given of the changes found in the various organs at all stages of the disease.

The chief features consisted of focal perivascular exudation, chiefly of lymphocytes, but sometimes of monocytes and fibroblasts, with vascular endotheliosis in the heart muscle, lungs and several other organs.

In the lungs small foci, " scarcely nodules," were found ; these were characterized by a sparse leucocyte and predominatingly epithelioid-cell exudate in the alveoli and by a lymphocytic and monocytic infiltration of the interstitial tissues. Later small granulomatous nodules made up chiefly of epithelioid cells were found and still later multinucleated giant cells were seen in some of the granulomata, which were most abundant in the spleen, liver and vertebral marrow.

Compared with epidemic typhus fever and even with Rocky Mountain spotted fever focal lesions in the brain and spinal cord of the guineapigs were strikingly infrequent. In most cases only occasional small foci of lymphocytic infiltration were found in the meninges or in the choroid plexus of one or more ventricles.

John W. D. Megaw.

GROOT (Hernando), MAYORAL (Pedro) & MARTÍNEZ (Luis E.). Resumen de observaciones y estudios sobre Bartonellosis. [**Studies on Bartonellosis.**]—*Rev. Facul. de Med.* Bogota. 1941. Nov. Vol. 10. No. 5. pp. 377–402.

YELLOW FEVER.

SOPER (Fred L.). **Treatment of Yellow Fever.**—*Jl. Amer. Med. Assoc.* 1942. Jan. 31. Vol. 118. No. 5. pp. 374–378.

A general account of the subject with special reference to the blood chemistry and metabolism of the disease, the clinical picture, and treatment. Whilst the situation with regard to prophylaxis is very

favourable, the therapy of yellow fever can be given in the words of Lins, " the disease cures itself or kills in spite of any and every treatment." Once yellow fever has declared itself there are no known specific serological or chemical agents of value, although there are certain clear indications for symptomatic treatment, and careful nursing is essential. *E. Hindle.*

MACKIE (F. P.). **Yellow Fever Prophylaxis.** [Correspondence.]—*Brit. Med. Jl.* 1942. Feb. 21. p. 270.

The writer of this letter, who is Chief Medical Officer, British Overseas Airways Corporation, draws attention to the fact that although the possibility of air transmission of yellow fever is great, it has never yet been proved that it has occurred. It is obvious that other methods of transport are liable to be incriminated ; the motor traffic between the Congo and Uganda and sea traffic between Africa and Asia have not yet received the attention they demand.

There is yet no uniformity in the regulations governing the period after protective inoculation at which persons are allowed to enter the various countries ; recent information shows that the periods are :—India 23 days, Uganda 14, Sudan 20, Kenya and Tanganyika 14, N. Rhodesia 15, Egypt 21 (believed now reduced to 14), Bahrein 21. Scientific evidence points to 14 days as an ample margin for safety and it is hoped that uniformity may be reached. The necessity for vaccination well in advance of departure from a yellow fever country is therefore evident. [In a comment on this letter HASLAM (*Brit. Med. Jl.*, 1942, June 13, p. 738) points out that in N. Rhodesia the period has always been 14 days, and that there is, therefore, complete uniformity among the African Dependencies usually referred to as the East African Group.] *C. W.*

RAND (Charles G.). **Immunity and Vaccination in Yellow Fever.**—*McGill Med. Jl.* 1941. Dec. Vol. 11. No. 2. pp. 11–19. [71 refs.]

A general account of the subject, dealing with the chemical and physical attenuation of vaccines, biological attenuation, the immune reactions produced by attenuated viruses, and, finally, the application of these in Public Health. The author concludes that, from epidemiological studies, it seems probable that despite these excellent means of prevention, yellow fever will remain endemic among certain species of jungle animals, ready to attack any traveller so unwary as not to be protected by vaccination. *E. Hindle.*

PLAGUE.

MEYER (K. F.). **The Known and the Unknown in Plague.**—*Amer. Jl. Trop. Med.* 1942. Jan. Vol. 22. No. 1. pp. 9–36. With 1 map. [70 refs.]

After a short introduction this article deals seriatim with the subject of the " known " and the " unknown " in plague, especially sylvatic plague :—

A. *The Known.*—(1) Sylvatic plague exists in 12 Western States of the U.S.A. (2) Localized epizootics in ground squirrels (Citellus)

and prairie dogs (Cynomys) with high mortality have been definitely attributed to plague, whereas tularemia and other diseases have been only sporadic. (3) These epizootics begin in spring, rise in intensity during summer, decline during autumn and disappear in winter if the rodents hibernate. (4) The epizootics may reappear periodically in the same area on the same ranch, but the factors determining this periodicity are not fully understood. (5) This periodicity of the epizootics led to the discovery of the persistence of sylvatic plague. The same burrows of infected squirrels yielded, 20 years later, plague infected fleas. "Thus plague persists indefinitely in an area once invaded." (6) The plague bacilli isolated in these epizootics are of the same biological type as those in other continents of the world, have more or less uniform infectiousness for mice and guineapigs and are not particularly pneumotropic. Strains of *P. pestis* isolated in California are Beta type, "glycerine-negative," "Oceanic Race" organisms in contrast to the Alpha type, "glycerine positive," "Continental Race." (7) Spontaneous infections or reservoirs exist among 31 rodents and rabbits in the Western part of the United States, of which 15 species belong to the ground squirrel Citellus genus. Prairie dogs constitute an independent reservoir in the Rocky Mountains. (8) Experimental infections have shown variations in the susceptibility of certain rodent species. It is argued that proven resistance of a given class of rodents is due to selection through the survival of naturally resistant individuals, but immunity due to a previous attack of the disease cannot be ruled out. (9) A pestiferous vector flea has been found to be indispensable to complete the propagation of plague among wild rodents. These fleas vary according to the rodent species and they vary also in their capability of accepting infection. The mode of transmission of plague by the wild rodent flea is the same as that for the rat flea. (10) Any form of contact of human being with the rodents of enzootic sylvatic areas is connected with a definite but somewhat limited risk of plague infection. The clinical features of the plague so contracted do not differ from those arising in cases derived from a rat source and, if pneumonic plague is excluded, there is a case mortality of approximately 50 per cent.

B. *The Unknown.*—(1) The appearance of plague among the wild rodents in North America was found relatively early by comparison with other endemic foci on the African, Asiatic and South American Continents. That these foci were really in sequence with the Hong Kong epidemic of 1894 is almost universally accepted. "The belief that plague is invariably imported is an ancient traditional concept somewhat similar to the superstitions which consider the pest a punishment from Heaven." (2) If the mode of arrival of plague to the inland of America is unknown it is only proper to inquire into its possible spread. "At some time or other, plague must have spread to occupy its present wide distribution" but "the distances between the various focal areas of rodent epizootics discovered during the past five years are enormous and contacts between different regions owing to mountains or deserts are absent." The agency of the flea vector is doubtless of prime importance. Cannibalism is not an established factor. Evidence of infection *per saltum* is not forthcoming, leaving the spread of the disease as due to contiguity. "The survey activities during the past 30 years have focussed . . . attention on the primary host—the squirrel, chipmunk or prairie dog" and only accidentally have data been secured concerning secondary spread to other rodents.

Little is known regarding the transmitting power and the species of wild rodent flea responsible for the occurrence of plague in human beings. (3) "Another important unsolved problem deals with the mechanism of persistence and perpetuation of rodent plague infection or the 'carry-over' from one season to another." Isolated data only are forthcoming either for the longevity of fleas or the length of time that fleas can harbour plague bacilli. (4) "There are a great many other unknowns which should be made the subject of analysis." Among these may be mentioned (*a*) the value of preventive vaccination; (*b*) the relative value of dead and living vaccines, of serum and of chemotherapy; (*c*) the value of different anti-rat measures."

"What may be theory to-day may become a fact to-morrow and *vice versa*." *W. F. Harvey.*

JUNIOR (Marcelo Silva). Observações à margem das "investigaciones sobre la peste en el nordeste brasileño" da autoria de Attilio Macchiavello. [**Observations regarding "Investigations on Plague in North-East Brasil."**]—*Brasil-Medico.* 1941. Nov. 15. Vol. 55. No. 46. pp. 762–771. With 1 chart & 1 fig.

HENRIQUES (Athos). Método de laboratório na profilaxia da peste. [**Laboratory Procedure in Plague Prophylaxis.**]—*Bol. Oficina Sanitaria Panamericana.* 1942. Mar. Vol. 21. No. 3. pp. 227–230. English summary.

All antiplague service should be centred round the laboratory which would concern itself with diagnosis, preparation of vaccines, epidemiology, rats and fleas.

Rats.—These are sent dead in 5 per cent. creolin or other insecticide solution. Fleas are removed for identification. At necropsy fragments of liver, spleen and lymph nodes should be taken up to a maximum of 30 rats, triturated under sterile conditions in a mortar, suspended in bouillon and inoculated on the scarified skin of rat or guineapig. These test animals may be subjected to Flit to kill their fleas.

Cages.—The animals remain in the cages until dead or until the 17th day after inoculation.

Bacteriology.—After death the inoculated animal is treated with Flit before autopsy. Smears are made from the lymph node, liver and spleen, to be stained by Gram's method. Culture is undertaken and then comes the verification of plague organisms as Gram-negative, vacuolated, non-motile bacilli, indole positive and giving a nitrite reaction with sulphanilic acid and α-naphthylamine. The main Pasteurella types to be differentiated are *pseudotuberculosis* which is motile, ferments rhamnose in 48 hours at 37°C. and is not pathogenic for white rats; *avicida* which ferments sucrose in 48 hours at 37°C. and produces indole; *pestis* which does not ferment rhamnose and sucrose in 48 hours, is non-motile, is pathogenic for white rats, does not produce indole, and which gives a nitrite reaction.

Fleas and Rats.—Require identification.

Transport of suspected material.—This may be in paraffin of melting point 42° to 44°C. Another very good method is to send the material in a test tube well covered and paraffined inside a thermos flask containing broken ice. Besides acting as preservative to the material the temperature of 0°C. inhibits the proliferation of other organisms,

but allows of slow increase of *P. pestis*. Broquet's medium (calc. carbonate 2 ; glycerine 20 ; distilled water 80) is a preservative of fleas and allows of isolation of the plague bacillus after 6 days.

W. F. Harvey.

MEDEDEELINGEN VAN DEN DIENST DER VOLKSGEZONDHEID IN NEDERLANDSCH-INDIË. 1941. Vol. 30. No. 3/4. pp. 158–213. With 5 graphs.—Verslag betreffende de pestbestrijding op Java over het jaar 1939. [**Annual Report on Plague in Java for 1939.**]

Most of this publication is of purely official interest as a record of the activities of Government plague services. It deals with personnel and districts and provides the tabular data of epidemiology, mortality and prophylaxis.

One of the notable antiplague measures which has been consistently pursued in the Netherlands Indies is that of improvement (primarily anti-rat) of the dwelling houses of the people. During the year this kept well ahead of the extension of plague, in that rebuilding was completed in six sub-districts while in only two did plague infection appear for the first time. The number of improved dwellings increased by 54,389 to a total of 1,579,753, and of new-built dwellings by 57,895 to 962,448. A noteworthy fact was the drop in the number of plague cases, 1,558 cases with 1,541 deaths in 1939, as compared with 2,107 and 2,083 deaths in 1938. Discussion naturally centres round the reasons for this fall. At least two factors seem to have been involved :—(1) the acceleration of vaccination and systematic revaccination, not to speak of an insusceptibility derived from repeated yearly vaccination, and (2) the later appearance of the rainy season and a specially dry period during November and December. During 1939 the number of vaccinations was 1,818,503, which brings the total injections of Otten's living vaccine up to 9,286,237. *W. F. Harvey.*

BACILLARY DYSENTERY.

POT (A. W.), VAN RAALTE (H. G. S.) & VAN DER SAR (A). Bijdrage tot de kennis der bacillaire dysenterie op Curaçao. [**Bacillary Dysentery in Curaçao.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1942. Feb. 10. Vol. 82. No. 6. pp. 234–250.

This is an account of the discovery of bacillary dysentery as a practically new disease on the Dutch West Indian island of Curaçao. Up to 1939 it seems to have been regarded officially as a rather unknown infectious disease. The mortality under the heading " diarrhoea and enteritis " gives the clue to the existence of the disease without its specific recognition. In the interval from 14th September, 1939, to 1st March, 1941, however, dysentery bacilli were cultivated 130 times from the stools of 118 patients. The types of dysentery were Flexner, Kruse-Sonne and Schmitz in descending order of frequency. As has been the case in Holland Shiga-Kruse bacilli have not been isolated. A connexion between degree of rainfall and the occurrence of dysentery has not been made out. This will require further investigation, but it may be that actual infections have their incidence some time after the rainfall itself. A point which is rightly stressed is the insanitary habit

of the population of Curaçao of defaecating in the open, but perhaps the mode of spread of dysentery bacilli is not by contamination of the drinking water, which is chlorinated, but by flies, so prevalent during the rains.

Table 4 relates in detail to 33 cases of dysentery and sets out the patient's race (white or coloured), age, the bacillary type, days before admission, intoxication, desiccation, acidosis, anorexia, tachycardia, left-shift of leucocytes, anaemia, number of days in hospital, duration of diarrhoea, complications and administration of serum. Clinical symptoms receive full consideration. Treatment consisted of: (1) Counteracting toxic symptoms by subcutaneous infusion of Ringer's solution with glucose in which at the same time high doses of vitamins C and B_1 were dissolved, (2) Vigorous administration of laxative during the first 24 hours, followed by dietetic measures, (3) sometimes serum and sulphapyridine. *W. F. Harvey.*

LAPPING (D.). **Chemotherapy in Bacillary Dysentery.**—*Indian Med. Gaz.* 1942. Feb. Vol. 77. No. 2. pp. 69–71.

Preliminary observations showed that sulphapyridine was effective in resistant cases of bacillary dysentery, so that a clinical trial on a large scale was undertaken. A total of 144 cases formed the subject of a comparison experiment. Most occurred on one estate.

Although facilities for complete bacteriological investigation were lacking, the stools were suggestive of bacillary dysentery; the majority were, clinically, Shiga infections. Cases were put on one of the following treatments :—

1. Polyvalent anti-dysenteric serum.
2. Sodium sulphate.
3. Sulphapyridine.
4. Sulphanilamide.

The last was discontinued after 19 cases had been treated, as not sufficiently effective.

Serum treatment—The smallest dose was 40 cc., some received over 100 cc. The intravenous route was employed wherever possible and, if necessary, glucose-saline was injected simultaneously.

Sulphapyridine—The smallest effective dose was 3 gm.; the average case required 8–15 gm. Commencing with 2 gm. and continuing with 1 gm. three hourly until general symptoms subsided.

The results were striking :—

Treatment	Number of cases	Deaths	Deaths per cent.
Serum...	38	2	5·3
Saline...	31	9	29·0
Sulphanilamide ...	19	4	21·0
Sulphapyridine ...	56	1	1·8

From these figures it was obvious that sulphapyridine constitutes an effective treatment for bacillary dysentery. The sulphapyridine

series comprised 56 cases and the only death was of a marasmic child of two suffering also from malaria. The drug relieves pain within 12 to 18 hours. The stool becomes normal within 3–7 days.

The earlier in the disease sulphapyridine is exhibited the quicker the response. *P. Manson-Bahr.*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

FAUST (Ernest Carroll). **The Prevalence of Amebiasis in the Western Hemisphere.**—*Amer. Jl. Trop. Med.* 1942. Jan. Vol. 22. No. 1. pp. 93–105. With 3 figs. (maps). [86 refs.]

The author has reviewed the records of amoebic infections in the Western Hemisphere; though these are far from complete certain conclusions can be drawn. Amoebiasis exists in an appreciable portion of the population from Central West Canada (52°30′ N. latitude) to the Strait of Magellan (52° S. latitude). It is much more intensely endemic in the American tropics than in the temperate zones. In areas like the United States the incidence may possibly average as high as 20 per cent., or double that of previously accepted estimates. A list of over 80 references concludes the paper. *C. M. Wenyon.*

WENRICH (D. H.) & ARNETT (John H.). **Results of a Protozoological Survey of Food Handlers at a Professional School in Philadelphia, Pa.**—*Amer. Jl. Trop. Med.* 1942. Jan. Vol. 22. No. 1. pp. 107–115. [18 refs.]

At a school in Philadelphia food-handlers were examined for intestinal protozoa each year for seven years, 1932–1939. This resulted in 50 older and more permanent employees being examined on an average 3·2 times and 140 student-helpers 1·4 times. When the results of the first examination alone are compared the employees gave a higher incidence for most infections than the student-helpers, who again had a higher incidence than did 1,060 freshmen previously reported upon. There was an exception with *Entamoeba histolytica,* which had an incidence of 10·7 per cent. amongst the helpers and 8 per cent. amongst the employees. The incidence obtained from the average of 3·2 examinations of the employees was considerably higher for most infections than that given by the single examination. The 21 cases of *E. histolytica* infection revealed no more gastro-intestinal symptoms than did others. *C. M. Wenyon.*

MELENEY (Henry E.). **The Duration of Human Infection with *Endamoeba histolytica* and Other Intestinal Protozoa.**—*Jl. Parasitology.* 1942. Feb. Vol. 28. No. 1. pp. 93–94.

Nine students who harboured *E. histolytica* were requested not to take any treatment, and were re-examined at various intervals. In two the infection persisted 4½ years, in two for 3½ years, in three for 1½ years. Further observations were not possible. Complement fixation tests were negative in seven of these students examined with an

alcoholic extract of motile amoebae as antigen and an anti-sheep haemolytic system, but four were positive when tested by CRAIG with his anti-human haemolytic system. *C. W.*

UNION OF SOVIET SOCIALIST REPUBLICS. REP. SCIENT. RES. WORK OF ALL-UNION INST. EXP. MED. [VIEM] FOR 1938–9. Moscow-Leningrad. 1940. pp. 114–115. [In Russian.]—[**Studies on Intestinal Protozoa.**]

In this summary an account is given of work carried out with human and simian intestinal protozoa in the Sukhum (Caucasus) laboratory of the Institute of Experimental Medicine. Attempts to infect the hamadryad baboon [*Papio hamadryas*] with human *Balantidium coli* and *Giardia intestinalis* failed. An Erivan strain of *Entamoeba histolytica* (pathogenic to 83 per cent. of infected kittens) produced diarrhoea in a new-born macaque [*Macacus rhesus*], but no symptoms at all in a new-born hamadryad baboon. *E. histolytica*-like amoebae isolated from various species of monkeys [unnamed], when inoculated into kittens, proved to be pathogenic to them, thus behaving like the human strains.

Investigations were also made on the influence of the intestinal flora upon susceptibility to infection with *E. histolytica*. In kittens and pups inoculated simultaneously with amoebae and dysentery bacilli the course of the disease was extremely severe ; after a short incubation period colitis developed, terminating in death after 3–5 days. On the other hand, in the controls inoculated with amoebae alone the percentage of infected animals was lower, the course of the disease not so acute, and pathologico-anatomical changes not so pronounced.

C. A. Hoare.

HOQUE (A. K. Makfuzal). **Intussusception caused by Amoebic Dysentery.**—*Indian Med. Gaz.* 1942. Feb. Vol. 77. No. 2. p. 95.

CHOPRA (R. N.) & CHOPRA (I. C.). **Treatment of Chronic Intestinal Amoebiasis. Use and Abuse of Emetine.**—*Indian Med. Gaz.* 1942. Feb. Vol. 77. No. 2. pp. 65–68. [13 refs.]

This paper is based upon 1,105 cases of intestinal amoebiasis treated by the senior author in the Carmichael Hospital for Tropical Diseases during the past 20 years.

Emetine injections are of little value in the treatment of chronic forms and of carriers. Its exhibition under these circumstances is a waste and abuse. Emetine is a toxic drug, and it is too often given without due precautions. It is not now considered to be so specific as formerly, and supplies are restricted on account of the war, so that great care is necessary in its administration.

The chief indications for parenteral emetine therapy are acute amoebic dysentery, and amoebic hepatitis with, or without, abscess formation, but even in the acute stage the quinoline derivatives, kurchi alkaloids and carbarsone have proved almost as effective.

Emetine injections are indicated when acute exacerbations arise in chronic amoebiasis, then 3 to 4 injections of 1 grain each control the symptoms.

In chronic amoebiasis good results were obtained with emetine bismuth iodide. One course may not be successful, and several in

increasing doses may have to be given. This drug has all the depressing and toxic effects of emetine, and has not proved altogether satisfactory in Indian patients.

On the other hand, carbarsone, yatren, enterovioform and kurchi alkaloid are on the whole beneficial. *P. Manson-Bahr.*

GARCIA PALAZUELOS (Pedro) & LERNER (Jacobo). Diagnostico y tratamiento del absceso hepatico amebiano. [**Diagnosis and Treatment of Amoebic Liver Abscess.**]—*Rev. Med. de Chile.* 1941. Feb. Vol. 69. No. 2. pp. 67–74.

JAMESON (J. E.). **Notes on Cases of Chronic Diarrhoea and Vague Ill-Health, apparently due to the Flagellate** *Giardia lamblia.*—*Jl. Roy. Army Med. Corps.* 1941. Dec. Vol. 77. No. 6. pp. 320–323.

The paper gives an account of seven cases of giardia infection associated with vague gastric disorder or frank diarrhoea with periodic remissions. The fact that in all these cases treatment with atebrin by the mouth got rid of the infection as well as the symptoms appears to indicate that the flagellate is not without pathogenicity, and that atebrin is a specific for the infection. *C. M. Wenyon.*

RELAPSING FEVER.

CHARTERS (A. D.). **Relapsing Fever in Abyssinia.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1942. Mar. 6. Vol. 35. No. 5. pp. 271–279.

A description of relapsing fever based on 32 cases, which, with one exception, all occurred at Soddu in the Lake District of Abyssinia during July 2nd to August 19th, 1941. The most outstanding clinical symptoms were hepatitis and dyspnoea. Neuritis was present in four cases. The cases were treated by injections of Neoiacol, an Italian arsenical preparation issued in two forms, one for intravenous and the other for intramuscular use. Intravenous injections in fairly large doses acted more rapidly in causing the disappearance of spirochaetes from the blood than either intramuscular or smaller intravenous injections, and no relapses occurred after the large doses. The examination of fresh coverslip preparations of blood was the quickest method of diagnosis. When fresh blood was negative, thick films were taken—up to 12 on one slide—and stained. This effects great economy in slides and stains. The intermediate host is assumed to be the louse, since spirochaetes were found in the gut of two *Pediculus corporis* caught on a patient's clothes. *E. Hindle.*

DAVIS (Gordon E.), WYNNS (Harlin L.) & BECK (M. Dorthy). **Relapsing Fever:** *Ornithodoros parkeri* **a Vector in California.**—*Public Health Rep.* 1941. Dec. 19. Vol. 56. No. 51. pp. 2426–2428.

Spirochaetes of relapsing fever have been found in *O. parkeri* collected in the Fresno, Kern and Stanislaus Counties of California, and the first case of human relapsing fever directly attributable to this

tick is reported ; all other cases in California have been reported from timbered regions at high altitudes, the typical habitat of *O. hermsi*. Spirochaetes have now been found in *O. parkeri* from California, Montana, Nevada, Utah and Wyoming, and the ticks have also been found in Colorado, Oregon and Washington. The habitat of some of the ticks was the sandy floor of a cave ; previously all other collections had been made from rodents and the burrows of rodents or burrowing owls. *C. W.*

LEPROSY.

LOWE (John), DHARMENDRA & SEN (N. R.). **Epidemiological and Clinical Studies of Leprosy in the Bankura District of Bengal.**—*Leprosy in India.* 1941. Oct. Vol. 13. No. 4. pp. 127–134.

A report on a study of the epidemiology of leprosy in a typical rural area in Western Bengal, which was commenced in 1936, was published in *Leprosy in India* in 1938 [see this *Bulletin*, 1938, Vol. 35, p. 883]. The enquiry has been continued with the following results.

A treatment centre was attended by about half the patients, but irregularly. Few of the infectious cases were isolated because of difficult local conditions. As the main object was an epidemiological inquiry no real attempt was made to control leprosy in the area and the work done can have had little influence on the leprosy position. A comparison with the situation four years ago may therefore be of value.

The total number of cases has fallen from 424 to 422 only and the incidence from 4·2 per cent. to 3·9 per cent. The proportion of lepromatous cases has declined from 22·6 per cent. to 21·1 per cent., not a significant change. There has been an increase in the proportion of lepromatous cases in children up to 14 years of age from 6 per cent. to 12 per cent. owing to the development of new cases in larger number than those who have moved into a higher age group. During the four years up to 1941, 59 of the original 424 patients have died ; 23 of these were lepromatous cases. The death rate in lepromatous cases was 25 per cent. against 11 per cent. in neural cases. Of 56 new cases 12 are lepromatous and 44 neural, 23 of the latter being children under 10 years of age, while practically all the new lepromatous cases were between the ages of 5 and 24. Of the 44 new neural cases 11 had shown suspicious lesions in 1937. Definite evidence of contact with an infectious case was obtained in 45, or 80 per cent. Of the 56 new cases, in 28 there was an infectious person living in the house, and in 17 more a definite history of extra-familial contact with an infectious case. Forty-one of the 56 new cases have been found in families in which one or more had already been recorded.

A striking fact is that out of 328 neural cases found in 1937 only two had become lepromatous by 1941 ; in addition one later discovered neural case had become lepromatous, all three being children living in contact with infectious persons. No adult neural case had changed its type. The majority of the adult neural cases were of the tuberculoid variety. Many of the lepromatous cases had become worse in addition to the 25 per cent. of deaths. The evidence indicates that 61 per cent. of the new cases originated early in life, but it does not point to leprosy

acquired in early life being more severe than that commencing at a later age. These observations afford interesting information on the natural progress of leprosy in a rural area under close observation during four years. *L. Rogers.*

GÓMEZ PLATA (Carlos). Ideas generales sobre la organización de la campaña antileprosa en el pais. [**The Leprosy Campaign in Colombia.**]—*Rev. Med. y Cirugia.* 1941. July. Vol. 8. No. 7. pp. 11–14, 17–19.

A very general account of the foci of leprosy in the country and the numbers in the two lazarettes Agua de Dios and Caño de Loro. At the former of these there are eight residents, five males and three females ; at the latter 145, of whom 106 are males and 39 are females. The municipalities in which lepers are found and their incidence per thousand inhabitants are said to be as follows : Campo de la Cruz 3·69, Manatí 2·83, Sabanalarga 1·22, Santo Tomás 1·2, Repelón 1·1, Barranquilla 0·3. *H. H. S.*

ARAUJO (H. C. de Souza). A lepra infantil na Colombia. Séde e typos das lesões iniciaes. [**Leprosy in Children in Colombia. Site and Type of Initial Lesions.**]—*Brasil-Medico.* 1940. Mar. 9. Vol. 54. No. 10. pp. 145–151. With 4 figs. & 4 graphs. [15 refs.]

The author mentions 25 cases and gives short details of 20 of them. The ages of the 20 range from 3 years to 13½ (nine only are under 8 years of age). All but one of the 25 started with achromic maculae—indicative, it is said, of a certain degree of immunity—one only presented an initial leproma. Line drawings show the sites of these initial maculae in each of the 20 patients ; most of them are on the trunk and lower limbs.

The author considers the question of congenital leprosy and mentions a child of 31 days with a circinate macula, a centimetre in diameter, over the coccygeal region, which the mother asserted had been present at birth, and three nodules which appeared a fortnight or so later, one over the left deltoid, one on the inner surface of the left thigh and one on the right leg. The author intended to watch these for some days before taking a piece for biopsy, but the mother became suspicious and disappeared, taking the infant with her. *H. H. S.*

ALBARRACÍN (Leopoldo). La lepra frusta. Descripción. Su significado epidemiológico. Una historia clínica. [**Abortive Leprosy. Its Epidemiological Significance.**]—*Bol. d. Inst. Nac. de Hig. Samper Martinez.* Bogotá. 1941. Dec. 2. No. 4. pp. 21–31.

The author describes the case of a white woman of 27 years born in a leper district which in the past ten years has furnished a number of lepers in whom the bacilli cannot be demonstrated. She presented on the outer and upper aspect of the left thigh a macule some 10 cm. in diameter, in which sensation to touch, heat and pain was absent. It had first appeared 15 years before, when she was 11 years old, as a small spot attaining its present size in about a year. About the same time her nose used to bleed and there was a nasal discharge for about 8 months. This ceased and there was found to be a perforation of the

nasal septum, 4 mm. in diameter with smooth edge; there was no deformity. The diagnosis is made from lupus and syphilis. Six members of the family with whom she lived were lepers.

Epidemiological study of the patients in this district indicate that the disease is undergoing a change, as though the subjects were acquiring a certain degree of immunity to the infection, and cases such as this, in which the disease seems to come to an end spontaneously after a short period, are increasing in number. *H. H. S.*

SLOAN (T. B. M.) & EBENEZER (Roy). **Skin Grafts in Leprosy.**—*Leprosy in India.* 1941. Oct. Vol. 13. No. 4. pp. 122–124. With 1 plate.

This is the record of a case in which, after an operation for the removal of necrosed bone from the great toe, sloughing of the skin over the ankle occurred with exposure of tendons. When healthy granulations had appeared the wound was successfully grafted with small portions of skin removed from the left thigh. The case is illustrated by a photograph taken after recovery. *L. Rogers.*

CHATTERJEE (K. R.). **A Conservative Method of removing Terminal Phalanges in Leprosy Patients.**—*Leprosy in India.* 1941. Oct. Vol. 13. No. 4. pp. 125–126. With 4 figs. (2 on 1 plate).

The author advocates a conservative operation in cases of necrosis of the terminal phalanges with a view to preserving as much as possible of the soft tissues and also the nails. For this purpose he makes a horse-shoe incision along the sides of the digit and over the end of the last phalanx, care being taken to preserve the nail bed which is included in the dorsal flap, with just enough soft tissue to maintain its nutrition; the ventral flap is formed by the pulp of the finger. After the necrosed bone has been removed the wound is sutured and a terminal drain inserted. Secondary infection rarely causes much trouble and the results are good. *L. Rogers.*

GOMES (J. M.). Lepra murina. Pesquizas com os pigmentos carotenoides. [**Murine Leprosy. Research with Carotene.**]—*Brasil-Medico.* 1940. Mar. 2. Vol. 54. No. 9. pp. 140–143. English summary.

For this investigation the author gave to 10 rats, by injection into the right flank, 0·5 cc. of a 0·2 per cent. colloidal emulsion of carotene, together with 0·5 cc. of an emulsion of Stéfansky's bacillus. Five of them were given 0·5 cc. of the carotene suspension weekly till 2·5 cc. had been given. Five were given the initial dose of carotene and bacillus but no after-doses of carotene. Five others were injected with the organism alone, as controls. One of each group was killed and examined on the 30th, 34th, 60th, 74th and 95th days. In the second and third groups the disease was found to have progressed naturally, the lesions being rather more active in the third, the control, group. In the first, the animals showed fewer bacilli and in the last one, killed on the 95th day, the organisms could be seen only in the liver and spleen, and here these were mostly fragmented. The author believes that the

carotene " stimulates the evolution of the bacilli," while it also stimulates the host's tissues to destroy the organisms in the early stage, the homogeneous acid-fast stage. *H. H. S.*

HELMINTHIASIS.

LIMA (A. Oliveira). Alergia em helmintologia. Sobre o valor dos testes cutaneous para o diagnostico das helmintiasis. [**Allergy in Helminthiasis : the Value of Skin Tests in Diagnosis.**]—*Brasil-Medico.* 1941. Dec. 27. Vol. 55. No. 52. pp. 845–848. [38 refs.]

The essence of this paper lies in the author's conclusions regarding the extent to which the helminthic antigens, whose preparation he describes, are reliable tests of the presence in the host of certain species of parasites.

As to trematode infections of man, positive skin reactions may be got in schistosomiasis when using an antigen derived from any mammalian schistosome or from *Fasciola hepatica* or *F. gigantea*, and extract of a liver containing Fasciola gives a positive reaction in those parasitized by Dicrocoelium. With cestodes an antigen got from any species will react with any member of the genus [but zoologists do not guarantee to retain any particular species in any particular genus]. With nematodes, Trichinella antigen gives positive reactions when there is infection with Trichuris ; the antigens of Ascaris and Trichuris differ, but a single antigen appears to cause reactions in all filariae. Instructions are given for the preparation of antigens. *Clayton Lane.*

RISQUEZ (Jesus Rafael) & BOZA (Fermin Velez). Nota preliminar acerca de algunas reacciones alérgicas observadas en casos de bilharziosis Mansoni. [**Allergic Reactions in Schistosomiasis Mansoni.**]—*Gac. Méd. de Caracas.* 1941. May 31. Vol. 48. No. 10. pp. 289–290.

In this preliminary note the authors state that an antigen was prepared from cercariae of *S. mansoni* obtained from washed *Planorbis guadeloupensis*. The full description of the method of preparation will be published later. This antigen was injected intradermally in a number (unstated) of persons of all ages, and as control an injection of the diluent, without the helminthic protein, was made. A positive reaction consisted of a zone of erythema with the formation of a nodule ; there were no systemic reactions. The local reactions appeared, sometimes as early as 20 minutes after the injection, sometimes as late as 24 hours.

In all the cases of schistosomiasis the test was positive ; in cases in which the disease was suspected it was positive in 92 per cent. ; in uninfected controls it was positive in 1 per cent. [definite figures of numbers tested are not given]. Further investigations are to be made ; in the meantime, the authors make no definite claims for this method as a diagnostic procedure. *C. W.*

JOHNSTONE (R. D. C.). **Acute Haemolytic Anaemia following Phenothiazine Therapy.** [Memoranda.]—*Brit. Med. Jl.* 1942. Feb. 21. p. 259.

The patient, a girl of seven, was given, for threadworm infection, phenothiazine, 1·0 gm. twice daily for five days, a total of 10 gm. Two

days after completion of this course she was admitted to hospital pale, jaundiced and dyspnoeic. The haemoglobin value was 42 per cent. Transfusion of two bottles of stored blood, followed by 1 pint of 5 per cent. dextrose, produced great improvement and next day the haemoglobin was up to 74 per cent.; the child recovered. Details of blood examinations are given. A sister of the patient had a similar but milder attack after the same dosage. The author points out that in 58 published cases of treatment with phenothiazine for threadworms, eight showed some form of toxic reaction; he considers that in face of such a high incidence the use of the drug cannot be justified.

C. W.

HOFFMAN (Wm. A.) & JANER (José L.). *Bufo marinus* **as a Vector of Helminth Ova in Puerto Rico.**—*Puerto Rico Jl. Public Health & Trop. Med.* 1941. Mar. Vol. 16. No. 3. pp. 501–504. [Spanish version pp. 505–509.]

The giant toad of Surinam, since it was introduced into Porto Rico from Barbados and Jamaica in 1920–1924 and thence into Hawaii, Mauritius and Louisiana, has satisfactorily fulfilled the object of its introduction by markedly lessening the numbers of white sugar cane grubs, but it has been found to pass on unharmed through its alimentary canal numbers of eggs of *Ascaris lumbricoides*, *Trichuris trichiura* and *Schistosoma mansoni*.

Janer noted the presence of eggs of *S. mansoni* in the faeces of "Sapos," as these toads are locally named, and on later examinations the writers have found eggs of roundworms, whipworms and schistosomes, all three species having viable specimens among them. The schistosome eggs are not the young of adults living within the toads; for careful dissections have revealed none, they and the other eggs have been swallowed by the frog. Larvae of Musca and Sarcophaga flies feed freely on human faeces and the great multiplication of these flies and their widespread breeding in faeces passed by promiscuous defaecation, provide links in the chain that carries the helminthic infections from man to man. *B. marinus* will eat these larvae and any ova contained within them and may thus pass on the ova. Yet it is believed that, all in all, *Bufo marinus* has brought to the island blessing far outweighing its drawbacks. Nevertheless it is at least a potential diffuser of certain helminthic infections, for of the faeces of 173 toads, 26 contained eggs of *S. mansoni*, 31 of *A. lumbricoides*, 28 of *T. trichiura* and 13 of hookworms.

Clayton Lane.

VOGEL (Hans). Ueber den Einfluss des Geschlechtspartners auf Wachstum und Entwicklung bei Bilharzia mansoni und bei Kreuzpaarungen zwischen verschiedenen Bilharzia-Arten. [**The Influence of Sex Partners on the Growth and Development of** *S. mansoni* **and in Cross Matings of Different Species of Schistosomes.**]—*Zent. f. Bakt.* I. Abt. Orig. 1941. Dec. 5. Vol. 148. No. 2/3. pp. 78–96. With 4 figs. [12 refs.]

In order to experiment on the sexual development of *Schistosoma mansoni* the author infected mice or hamsters with male or female cercariae or with both sexes and checked his work by cross-fertilizations between males and females of different schistosome species.

The solitary male of *S. mansoni* developed to sexual maturity and reached the same size as did a paired male worm, but the solitary male of *S. japonicum* did not. The solitary female of *S. mansoni* did not develop to sexual maturity and her size remained less than that of the paired female. The developmental influence of the male *S. mansoni* on the female of that species begins with pairing, while with *S. japonicum* the influence is mutual; this difference is not due to any difference in the host and its nature is unknown. It may be due to a hormone passing from worm to worm through the skin of genital secretions.

In further experiments the following cross-fertilizations were effected the male being cited first—*japonicum=mansoni*, *mansoni=japonicum*, *haematobium=mansoni*, *mansoni=haematobium*, *japonicum=haematobium*. In all cross-fertilizations there was pairing and copulation, and while the growth of the males might thereby be favoured, unaffected, or hindered, that of the females was always favoured, so the influence of the male was not specific. The eggs were never deformed, but always had the shape of those normally passed by the mother worms. *Clayton Lane.*

KRAKOWER (C.), HOFFMAN (W. A.) & AXTMAYER (J. H.). **The Fate of Schistosomes** (*S. mansoni*) **in Experimental Infections of Normal and Vitamin A Deficient White Rats.**—*Puerto Rico Jl. Public Health & Trop. Med.* 1940. Dec. Vol. 16. No. 2. pp. 269–345. With 27 figs. [20 refs.] [Spanish version pp. 346–391.]

White rats were infected by immersion in water containing cercariae from *Australorbis glabratus* and were thereafter maintained on a diet which was either normal, or was free from vitamin A, with or without the supplement of one drop of cod liver oil; time was then allowed for the parasites to reach the liver.

"In rats on the normal diet there was marked destruction of the parasites in the liver, maximum between the 5th and 7th weeks after infection. Thereafter parasites continued to be destroyed in liver and lung until there were few remaining viable worms at the end of the experimental period.

"In rats on the vitamin A free diet such destruction of the parasites was either absent or minimal. Even with the supplement of a drop of cod liver oil there was relatively little parasitic destruction up to the end of the 6th week after infection. Thereafter greater numbers of dead worms occurred, but still appreciably less than in rats on the normal diet for the same length of time after infection."

"It seems therefore that the chief mechanism of destruction of the schistosomes in the rat on the normal diet is due primarily to the migration of the parasites into narrow blood vessels such as the peripheral branches of the portal vein or the small arteries of the lung. If these are capable of widening to a degree which will permit the parasites to move freely within them, without close parietal contact, then it is unlikely that the worms will be destroyed except for reasons like that of oviposition described above. Usually, however, these vessels are incapable of enlarging to any extent, particularly in earlier stages of infection and the close and continued contact of their parietes with the parasites induces sharp reactive changes which serve to immobilize, fix and subsequently to destroy the worms. There was no evidence that any precipitin immune effect either about cuticle, oral parts or in the ceca occurred in the way described by Sarles and Taliaferro and Sarles in the case of *Nippostrongylus muris*."

"While the deficiency of the vitamin A factor in the diet permits excessive proliferation of less highly organized cells such as fibroblasts and histiocytes, it retards the resolution of lesions formed chiefly by these elements

(although the foreign body such as the dead parasite may be rapidly digested). It also retards the proliferation of more highly organized cells such as those of the parenchyma of the liver, over and above the minimal requirements of immediate regeneration.

"In schistosomal infections of the rat it is estimated that a maximum of 24 per cent. and an average of 11 per cent. of the cercariae to which the animal is exposed will reach the liver. Loss of cercariae through failure to penetrate the skin and beyond that in the complicated pathways until it reaches the liver accounts for this relatively low percentage.

"A modification of the slide method for the examination of *Trichinella Spiralis* was employed, which is adaptable for determining live and dead worms in the tissues of the infected host. It should be applicable to related studies in other helminthic infections."

Clayton Lane.

VOGEL (Hans). Infektionsversuche an verschiedenen Bilharzia-Zwischenwirten mit einem einzelnen Mirazidium von *Bilharzia mansoni* und *B. japonica*. [**Investigations on Different Intermediate Hosts of Schistosomes infected with a Single Miracidium from** *Schistosoma mansoni* **and** *S. japonicum*.]—*Zent. f. Bakt.* I. Abt. Orig. 1941. Nov. 5. Vol. 148. No. 1. pp. 29–35. [13 refs.]

The snails used were laboratory bred. Each was infected with a single miracidium, each *Planorbis guadaloupensis* or *P. pfeifferi* with one of *Schistosoma mansoni* and each *Oncomelania hupensis* with one of *S. japonicum*. Regarding *S. mansoni*, the African intermediate host, *P. pfeifferi*, showed greater susceptibility to this sort of infection than did the New World host *P. guadaloupensis*, a difference not so obvious when many miracidia are used to infect at the same time. This observation points to Africa as the original area of this infection. *P. pfeifferi* was infected with equal ease by a miracidium whether this came from an African or an American source.

Altogether 63 Planorbis snails were submitted to infection, each by a single miracidium of *S. mansoni*; of them 48 became infected, 25 with males and 23 with females. Similarly, of 27 Oncomelania snails submitted to infection each with a single miracidium of *S. japonicum*, 25 became infected, 12 with males and 13 with females. In both cases the proportion was close to 1 : 1.

The sex was determined by infecting mice with cercariae which in due course escaped from the snails, for the cercariae showed no difference in appearance distinguishing sexes. *Clayton Lane.*

KOPPISCH (Enrique). **Studies on Schistosomiasis Mansoni in Puerto Rico. VI. Morbid Anatomy of the Disease as found in Puerto Ricans.**—*Puerto Rico Jl. Public Health & Trop. Med.* 1941. Mar. Vol. 16. No. 3. pp. 395–455. With 36 figs. [26 refs.] [Spanish version pp. 457–500.]

The material came from 1,009 consecutive necropsies in San Juan, in which place there are no collections of water known to be infected with schistosome larvae, and from 18,500 tissue specimens taken from operative material or from partial necropsies. Of the former 147 and of the latter 99 disclosed eggs of *Schistosoma mansoni*.

"The fundamental histopathologic unit of the disease is the pseudotubercle, developing about ova. The development of pseudotubercles is traced from the early stage of eosinophilic and polymorphonuclear response

through that of an epithelioid cell nodule to the final healed fibrous body. There are, in addition, chronic inflammatory changes leading ultimately to fibrosis, especially in the liver and colon.

"From the beginning, the disease is primarily hepatic and colonic. Pathologic changes are instigated mainly by the deposition of ova in the tissues; in the colon this leads to colitis and in the liver to cirrhosis, which is periportal in distribution. Splenomegaly develops, in part at least, secondary to portal obstruction.

"The involvement of the liver and colon, and of other viscera, increases rapidly with the severity and duration of the infection.

"The main anatomico-pathologic alterations due to schistosomiasis, as found in this series, are divided for purposes of description into: cirrhosis, splenomegaly, colitis, pulmonary alterations, ascites, esophageal varices, retroperitoneal fibrosis, sclerosis and thrombosis of the portal vein and tributaries, bilharzial pigmentation, subserosal nodules of intestines, evolution of the pseudotubercles, and inflammatory changes due to schistosomiasis.

"The similarity of the late stages of schistosomiasis to the Banti syndrome is emphasized; likewise the need for thinking of this disease in all cases presenting that syndrome, or evidences of cirrhosis, or gastrointestinal symptoms, whenever the subject has lived in areas of endemic bilharziasis."

Koppisch draws special attention to two deaths in a pulmonary infection and particularly to one in a girl of 14. Her sputum had sometimes been blood stained, and there had been coughing, night sweats and some fever. The cough became more marked after her eighth fouadin injection, dyspnoea and cyanosis came on 12 hours later and she was dead in half an hour. At necropsy there were miliary bilharzial tubercles evenly distributed throughout both lungs, and in certain sections necrotic worms were visible within the veins. [Were they not, as is seen in the dog with Dirofilaria so treated, embolic dead worms lodged in pulmonary arterioles after being killed by fouadin? Compare also SHAW and GHAREEB this *Bulletin*, 1938, Vol. 35, p. 665.]

Clayton Lane.

DAENGSVANG (Svasti) & MANGALASMAYA (Montri). **A Record of Some Cases of Human Infestation with *Fasciolopsis buskii* occurring in Thailand.**—*Ann. Trop. Med. & Parasit.* 1941. Oct. 21. Vol. 35. No. 1. pp. 43–44.

A boy of six years had persistent diarrhoea, persisting abdominal swelling with ascites and enlarged visible veins, and oedema of the abdominal wall, face, scrotum and lower limbs. With a good appetite he wasted, his stool being watery with undigested food in it as well as many eggs of *Fasciolopsis buskii*. His body was stunted and his mind dull. Red cells numbered 3,290,000, eosinophils 6 per cent. and the haemoglobin was 65.

He had three treatments; the first two were with 0·3 cc. of oil of chenopodium every hour for three doses, followed by half an ounce of saturated solution of magnesium sulphate, the second followed the first after an interval of 14 days. A third treatment was by "an unofficial but well-known native anthelmintic." The worms recovered numbered respectively 141, 50, and 30; they varied in size but all were identified as *F. buskii*. Several later faecal examinations showed no ova. He was the son of a gardener who cultivated water-caltrops. The authors' interest led to the examination of the stools of the boy's family, which contained the same eggs in the following numbers to the gramme of formed stool:—mother 18,600, father 14,500, brother aged four 5,000,

brother aged two and a half 4,500, aunt 3,200. All but the last suffered from mild gastro-intestinal disorders, and were treated with the Thai drug. [It is regrettable that no hint of its identity is offered.]

Clayton Lane.

SCOLARI (Pedro G.) & OCAÑA (Tomas). Distomatosis cutanea. [**Cutaneous Distomiasis.**]—*Rev. Argentina de Dermatosifilologia.* 1941. Vol. 25. Pt. 3. pp. 369–376. With 5 figs.

A girl of 10 had shown a number of fugitive swellings under the skin on the right side of the lower abdomen and buttock. These finally proved to be due to a distome.

A swelling seen by the authors was about as big as a pigeon's egg, was adherent to the skin in the lumbo-gluteal region but moved freely on the underlying parts. The skin over it was normal in colour but looked like orange peel. It was neither painful nor tender. Under local anaesthesia by ethyl chloride the tumour was excised, in it lay a red clot, and in that a parasite measuring $7 \times 4 \times 1$ mm. This was light yellow in colour and had two suckers, one at the head end, the other at the junction of head and middle thirds [perhaps an attempt to determine its species will be reported later]. The host's tissue round it is described as having the character of a pyogenic and necrosing granuloma. Literature of other findings is mentioned but there are no definite references to it.

Clayton Lane.

BONNE (C.). Vier echinostomen van den mensch in Nederlandsch-Indië. *Euparyphium ilocanum* (Garrison 1908). *Echinostoma lindoensis* (Sandground en Bonne 1940). *Euparyphium malayanum* (Leiper 1911). *Euparyphium recurvatum* (v. Linstow 1873). [**Four Echinostomes of Man in the Netherlands Indies.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1941. June 24. Vol. 81. No. 25. pp. 1343–1357. With 1 plate. English summary. [16 refs.]

"Four echinostome parasites of man are known in the Malayan Archipelago:

Euparyphium ilocanum (Garrison 1908) in Java.

Echinostoma lindoensis Sandground & Bonne 1940 in Central Celebes.*

Euparyphium malayanum (Leiper 1911) in Northern Sumatra.

Euparyphium recurvatum (v. Linstow 1873) in Java.

"E. ilocanum is not uncommon in Java amongst inmates of insane asylums, where occupational therapy with agricultural work is practised. The mental deficient patients are prone to eat any insect or snail, that attracts their attention, including the snails of the ricefields harbouring echinostome-metacercariae. Its reservoir host is the field rat.

"E. lindoensis is extremely common in a few small villages, inhabited by a primitive Toradja tribe on the shores of Lake Lindo in Central Celebes. Infection takes place by consuming mussels (Corbicula lindoensis) from the lake, which contain the corresponding metacercariae. No reservoir host is known. This species has the largest size.

"E. malayanum was found (±750 specimens) at an autopsy of a Batak girl of 12 years in Northern Sumatra, by KLEIN, ESSEVELD and

* *Echinostoma lindoense* would seem to be a more grammatical name.—*Ed.*

KOUWENAAR and identified as malayanum by the author. Nothing is known about its modus of infection in Sumatra. This is the broadest species.

"E. recurvatum was only found once (±20 specimens) in a lunatic in Java together with E. ilocanum. Its reservoir host is probably the field rat.

"It is quite possible that these echinostomes have a more general distribution in the Archipelago, especially ilocanum.

Diagnostic table for the four species.

	Ilocanum	Lindoensis	Malayanum	Recurvatum
Length	4–10 mm.	13–16 mm.	5–10 mm.*	2·5–5 mm.
Width	0·5–1·5 mm.	2–2·5 mm.	2·2–3·5 mm.*	0·4–0·7 mm.
Number of circumoral spines† ...	51	37	43	45
Length of circumoral spines ...	30–45 μ	70–85 μ	50–70 μ	30–80 μ
Anterior border of vitellaria ...	Far posterior to acetabulum	Near hind margin of acetab.	Level with acetabulum	Posterior to acetabulum
Testes	Rounded or with indications of lobes	Lobes more distinct	Extreme development of lobes‡	Rounded or with indications of lobes
Cirrhus pouch ...	Reaching halfway acetabulum	Reaching very little beyond anterior margin of acetabulum	Reaching beyond posterior margin of acetabulum	Reaching halfway acetabulum
Average length of eggs	103 μ	101 μ	137 μ§	91·5 μ
Average width of eggs	59·5 μ	69 μ	75·5 μ§	57 μ

* Dependent on contraction and fixation.
† The number of circumoral spines is subject to slight variation.
‡ Nothing like the very deeply and broadly incised testes of malayanum is ever seen in the other species.
§ The eggs of malayanum are easily recognized by their large size.

MICHIGAN PUBLIC HEALTH. 1941. Aug. Vol. 29. pp. 153–155. **Swimmers' Itch as a Problem of Northern Resort Lakes being met by New Program of Chemical Treatment.** [Summary taken from *Public Health Engineering Abstr.* Washington. 1941. Dec. Vol. 21. No. 12. p. 54. Signed F. F. ALDRIDGE.]

Swimmers' itch, a problem of the lake resorts in Michigan and its neighbouring States, is characterized by inflamed skin areas and an intense itching that lasts generally from 4 to 7 days. Snails carry minute parasites known as Schistosome cercariae which burrow into the swimmer's skin. The larvae of adult worms living in the abdominal veins of muskrats and various waterfowl are spread by defecation into the water, thereby entering the snails and developing into the tiny wiggling cercariae. There are 3 possible control measures, namely :—

(1) Killing the muskrats and waterfowl.
(2) Killing the parasites after they leave the snails.
(3) By killing the snails.

Since the third method is the most practical, it has now been used successfully for three successive summers in Michigan's northern bathing beaches. The treatment consists of spreading a mixture of copper

sulfate and copper carbonate (two parts of copper sulfate and one part of copper carbonate) on the beach bottom by means of a power-driven pump and hose distributing equipment mounted on a boat. Since snails are sensitive to small quantities of copper they can be killed without harming the fish. An area of 1,000 square feet requires only 3 pounds of the above mixture, the cost of materials generally being estimated at 15 to 20 cents per foot frontage of beach covered.

McMullen (Donald B.) & Brackett (Sterling). **The Distribution and Control of Schistosome Dermatitis in Wisconsin and Michigan.**—*Amer. Jl. Trop. Med.* 1941. Nov. Vol. 21. No. 6. pp. 725–729.

There is no fully satisfactory method for killing, in wide stretches of water, the snails which are the intermediate hosts of those cercariae which cause bathing dermatitis.

Further knowledge of the habits and natural enemies of these snails and of the life cycles of the flukes concerned may suggest better methods of their control. In the meantime the fish-killing possibilities of copper sulphate have been greatly over-emphasized, for a concentration of from 10 to 100 parts per million has been introduced into portions of these lakes with nothing but a temporary effect on local fish ; and any deficiency of these numbers is soon made good by those which come into the treated area from outside. The broadcasting of copper sulphate crystals was the simplest method of control used, but its effectiveness diminished in water over two feet in depth, and the combining of two parts of copper sulphate and one part of copper carbonate, using three pounds of the sulphate-carbonate mixture per 1,000 square feet, gave better results in the deeper water. The use of copper sulphate alone in shallow water, up to two feet in depth, helped to reduce the cost of the treatment. Repetition yearly of copper sulphate is essential. Until the problem is permanently solved the tourist and holiday industry is threatened, serious outbreaks in boys' and girls' camps being particularly troublesome. *Clayton Lane.*

Union of Soviet Socialist Republics. Rep. Scient. Res. Work of All-Union Inst. Exp. Med. [Viem] for 1938–9. Moscow-Leningrad. 1940. pp. 113–114. With 2 figs. [In Russian.]—[**Life-Cycle of** *Diphyllobothrium minus.*]

One of the parasitological expeditions of the Institute of Experimental Medicine was engaged during 1938 and 1939 in helminthological investigations among the population of Lake Baikal. The present summary of unpublished work contains the first account of the complete life-cycle of *Diphyllobothrium minus*, a little-known human tapeworm first described by Cholodkovsky (1916) and since found to be endemic in the Baikal region. The coracidium hatches from the egg in the water and is ingested by *Cyclops strenuus*. In the body-cavity of the copepod the first larva gives rise to a procercoid which differs in structure from the corresponding stage of *D. latum*. The infected copepod is eaten by fishes, two species of lavaret and one grayling [presumably *Coregonus migratorius*, *C. lavaretus pidschian* and *Thymallus arcticus baicalensis* (Salmonidae)]. The plerocercoid develops on the outer walls of the inner organs, chiefly on the intestine, of the fish. Man and other carnivorous animals become infected by eating fish containing living plerocercoids.

In view of the fact that the local Mongolian population consume fish frozen, salted or slightly grilled, the viability of the plerocercoids was tested under these conditions. It was found that at a temperature of −20°C. they remain alive for 48 hours; when salted they live 8–10 days; while in grilled fish they may survive for 20–30 minutes.

C. A. Hoare.

i. SEGAL (L. J.). **Cysticercosis Epilepsy treated with Sulphathiazole.** [Memoranda.]—*Brit. Med. Jl.* 1941. Nov. 15. p. 693.

ii. LEIPER (R. T.). **Diagnosis of Helminth Cysts in the Brain.** [Correspondence.]—*Ibid.* Nov. 29. p. 787.

i. Segal reports that a man of 29 was found unconscious and admitted to hospital where, after examination, a diagnosis of hydatid of the brain was made.

He had served in the Navy, at one period on the China station, and there suffered from "a tropical disease." There set in mental depression and headaches which, on seven occasions, passed into unconsciousness and fits with complete amnesia of the incident [so that his statement rests on what he was told about himself]. Of symptoms pointing possibly to the brain there were mental dulness, a demand for sleeping tablets though he was asleep before they could reach him, blurring of the discs on the nasal side, and knee and ankle jerks somewhat increased especially on the left. There was 6 per cent. eosinophilia; spinal pressure on puncture was slightly increased but was not measured exactly; the Wassermann reaction was negative. X-rays showed in the left lung a cyst, of about the size of a five shilling piece, and a suggestion of an infected left maxillary antrum. Treatment with sulphathiazole gave great mental improvement. After a second course the eosinophilia disappeared.

ii. Leiper points out that, with title of epilepsy from cysticercosis, the text gives a diagnosis of hydatid disease, and suggests that the combination of the China station and a tropical disease point to infection with *Schistosoma japonicum* and call even yet for an examination of the faeces for these eggs.

Clayton Lane.

DAVSON (J.). **Malignant Hypertension Associated with Hydatid Disease of the Kidney.**—*Jl. Path. & Bact.* 1941. Sept. Vol. 53. No. 2. pp. 207–212. With 4 figs. on 1 plate. [23 refs.]

"It has been shown experimentally that constriction of one renal artery will produce persistent hypertension with development of the characteristic lesions in the opposite kidney, but not in the constricted organ. This case appears to furnish a close analogy with these experimental findings."

A woman of 25 died with a clinical diagnosis of chronic nephritis, and necropsy showed a suppurating hydatid cyst in the right kidney and a characteristic histological picture of malignant hypertension in the left. Her illness had lasted about two years, her blood pressure had been 220 mm. of mercury, but in hospital it was 200/100, the urine showed 2 mgm. of protein to the litre, and the blood 196 mgm. of urea in 100 cc. on admission, rising to 378 at her death 10 days later. At necropsy the *right* kidney showed at its lower pole a suppurating hydatid cyst, measuring 6 by 5 cm. containing necrotic scolices, a dilated renal pelvis with gross compression of the renal substance, partial obliteration of moderate sized branches of the renal artery, and fibrosis of the

renal parenchyma. The *left* kidney showed a histological picture characteristic of hypertension—the glomeruli nearly normal in number, but few being normal in structure; about a quarter had focal necrosis, many showed hyalinization, a few were completely fibrosed, and a number exhibited capsulitis and some haemorrhagic infarction; the tubules were generally degenerate, groups of convoluted tubules were full of red cells, many contained hyaline casts; afferent arterioles showed necrotizing inflammation or intimal fibrosis which might close the lumen; the larger branches within the kidney showed no change.

Clayton Lane.

García Capurro (Federico). Diagnóstico radiológico de la membrana hidatídica encarcelada importancia del signo de Ivanissevich. [**X-Ray Diagnosis of the Retained Hydatid Membrane; the Importance of Ivanissevich's Sign.**]—*Bol. Inst. Clin. Quirúrg.* Buenos Aires. 1941. June–July. Vol. 17. No. 141. pp. 303–320. With 18 figs.

This paper emphasizes, with X-ray plates and diagrams, the condition reported by Iturraspe [this *Bulletin*, 1940, Vol. 37, p. 588]. In a hydatid of the lung which has opened into the bronchial tree, but in which the parasitic membrane and part of the fluid has been retained, the X-ray plates show a different appearance according to the direction in which the picture has been taken. It is only when taken laterally that the cavity shows a polygonal outline. *Clayton Lane.*

Heilig (Robert). **Practical Aspects on General Anasarca, especially in Malarial Nephritis and Hookworm Disease.**—*Indian Med. Gaz.* 1941. Sept. Vol. 76. No. 9. pp. 519–523.

At the Krishnarajendra Hospital, Mysore, ascites-anasarca cases are many. They fall into three groups and their differential diagnosis as a guide to treatment is of vital importance. The common causes are heart failure, nephritis and hookworm infection.

Heart failure is due to valvular disease or hypertension; the latter is frequent among Brahmins, strictly vegetarian for generations, and is not discussed.

The nephritis is an acute or subacute glomerulo-nephritis. Of six acute cases admitted over a period of 8 months and beginning characteristically as oedema of the eyelids and face, four were young girls with acute malaria, two tertian and two subtertian, and the oedema, albuminuria and haemoglobinuria, as well as the ordinary malarial symptoms subsided under quinine. The subacute cases gave a history covering a few months and showed albumen 0·25 to 3 per cent., casts of every sort and red cells and a specific gravity nearly always between 1015 and 1018; [systolic] blood pressure in half the cases lay between 135 and 160, the diastolic being normal; a large spleen floated in the ascites. Quinine in full doses got rid of the fluid, a table showing a loss of body weight of nearly 30 lb. in 13 days.

The most frequent cause of the anasarca is hookworm infection. The patients show a waxy, grey, puffy face, tongue and palate looking like grey paper, in the abdomen 25 or more pints of straw-coloured fluid nearly free from protein and with a specific gravity of 1006, the legs and scrotum swollen. The heart signs are those of double mitral

disease, but there is no dyspnoea or orthopnoea, no enlarged liver and no subicterus. The blood often shows haemoglobin 10 to 12 per cent. to Sahli, the urine is normal unless there is complication.

" In these hookworm cases exists only one line of rational treatment: to improve the blood condition so far that carbon-tetrachloride or tetrachlorethylene can be given without risk. Though hookworm anaemia is known as a typical microcytic-hypochromic anaemia that simply has to improve quickly on administration of sufficient doses of ferrous iron, some of our patients do not follow this rule. We give in every case 90 grains of freshly prepared Blaud's pills per day and the effect is practically always a quick improvement from Sahli 12 to 18 or 20, but from this level upwards the blood improvement progresses quickly and satisfactorily only in the majority of our cases, not in all of them. A minority remains that requires crude liver extract for further improvement; these cases are characterized by a comparatively high colour index of about 0·8, whereas the simple iron deficiency anaemias have an index of about 0·35 to 0·5."

With this iron, and if necessary liver treatment, is combined to save time this diuretic: ammonium chloride grains xx, calcium chloride grains v five times, and urea grains v three times, a day. Usually this treatment for three weeks raises the haemoglobin to 35 or 40 per cent. and then anthelmintic treatment may safely be given "yielding innumerable hookworms (*Necator americanus*)." After this, cure is not accepted until 3 motions passed on alternate days are free from hookworm eggs.

The importance of recognizing this infection is stressed in these words " apparently nowhere else—neither in Iraq nor in America nor even as near as the Madras Presidency, are such desperate looking cases of hookworm disease to be found as we see here every day."

[Such anasarca cases will be found described and pictured in the Second Annual Report of the Rockefeller Sanitary Commission for the Eradication of Hookworm Disease for 1911; and in Vol. 59 of the U.S. Senate Documents are reports by ASHFORD and IGARAVIDEZ with printed and pictorial evidence of the same kind for Porto Rico. To these hookworm campaigns of 30 years ago, Porto Rico and the southern of the United States of to-day owe much. May the India of 30 years hence owe as much to the India of to-day.] *Clayton Lane.*

DE SARAM (G. S. W.) & GUNEWARDENE (S. R.). **An Analysis of Forty-Two Cases of Death following Anthelmintic Treatment.**—*Jl. Ceylon Branch Brit. Med. Assoc.* 1941. Sept. Vol. 38. No. 3. pp. 255–294.

Between 1927 and 1936 there were administered in Ceylon 22,517,766 hookworm treatments with 42 officially reported deaths [about two in a million]. Even if the figures of deaths are not fully complete the death rate was very small, further care may lessen it and mass treatment should be strongly pushed.

Of the 42 deaths, 33 were of children up to 13 years old, the other 9 were of persons between 17 and 65; in the children death occurred as early as 10 minutes and as late as 5 days after treatment. Every death is dealt with in text and table, but details disappoint. Case 42, a lad of 17, is said in the text to have been given " 1 oz. " of tetrachlorethylene and in the table " dr. z," yet for a man of 40 the reported dose was ♏xxv. It is believed that some of the deaths resulted from concentrated magnesium sulphate solution given to the weak. *Clayton Lane.*

HALA (H. L.). **Effect of Sulphapyridine on Roundworms in a Child with Pneumonia.**—*Indian Med. Gaz.* 1941. Aug. Vol. 76. No. 8. p. 482.

A child treated for bronchopneumonia with sulphapyridine (one half of a tablet [presumably 0·25 gm.] every 4 hours for two days, and in reduced doses for the next five days) passed 148 roundworms [*Ascaris lumbricoides*] on three successive days. Stool examinations carried out two weeks later showed no ova. The author suggests further investigations since he has found treatment with santonin to be unsatisfactory.

C. W.

BRICK (Miriam A.) & DONOHUE (W. L.). **Granulomatous Lymphadenitis caused by Filariae.**—*Canadian Med. Assoc. Jl.* 1941. Oct. Vol. 45. No. 4. pp. 315–317. With 4 figs.

A child of 4, born in China, had been in Canada for six months, and was suspected of being tuberculous, having enlarged lymph nodes in the right axilla. These were excised and the condition displayed was found baffling till a section of a female *W. bancrofti* was seen.

The worm's surroundings were as they usually are, and a microfilaria was also found. Whether the blood was later examined at night is not stated; earlier examination had shown an eosinophilia of 58 per cent., after operation it dropped to 2 per cent. She had frequent evening rises of temperature to 100° or 101°F.

Clayton Lane.

i. EARLE (K. Vigors). **The Use of Sulphonamide Compounds in Filarial Complications.**—*Med. Jl. Australia.* 1941. Aug. 23. 28th Year. Vol. 2. No. 8. pp. 200–202. With 2 charts. [13 refs.]

ii. ——. **Filariasis of the Breast: a Mammographic Study.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1942. Jan. 31. Vol. 35. No. 4. pp. 235–236. With 4 figs. on 2 plates.

i. Sulphapyridine [M. & B. 693] was tested for this purpose on Nauru Island, Central Pacific.

During these complications microfilariae were present in blood films throughout the attacks. There are described: three cases with lymphadenitis and lymphangitis, one of funiculitis with scrotal cellulitis, one of mastitis and one of teno-synovitis in the left forearm. All these reacted to the drug which was given every four hours, two tablets for the first two doses and one for each of 9 to 11 more, and in all cases the effects were striking. In one case of myositis and in two of "filarial abscess" good could not be attributed to the drug.

ii. The case described above as mastitis is here concerned. When the acute attack had subsided the affected breast (right) was X-rayed.

This was one of many attacks in a woman of 52 in one of which the breast had been incised. In this attack it was enlarged, the skin was red and tender and in one place tense with "orange skin" appearance, the nipple enlarged and hard, a tender mass in the upper and outer quadrant, an enlarged tender lymph node just under the edge of right pectoralis major, the axillary nodes were normal; microfilariae were found in night blood, X-rays showed increased density from fibrosis. Later, injections of lipiodol into the openings of the mammary ducts at the nipple showed uniform patency and ramification.

Clayton Lane.

EARLE (K. Vigors). **Further Experiences with Sulphapyridine in Filariasis.**—*Lancet.* 1941. Nov. 29. pp. 667–668.

"The strikingly beneficial effect of sulphapyridine on the lymphadenitis complicating filariasis probably indicates that the complication is due to secondary streptococcal infection rather than to the filariasis itself." The author quotes two cases, of lymphangitis and of cellulitis, in which rapid relief was brought about by this drug. In a third case, of filarial myositis, sulphapyridine was ineffective but recovery followed incision and the evacuation of dark greenish pus. Such pus is usually sterile and is regarded as filarial in origin, thus differing from that found in true tropical pyomyositis, in which staphylococci are usually present. *C. W.*

NETTEL (Roberto). Onchocercosis. Los nodulos de localización dificil. (*Onchocerca caecutiens* Brumpt.) [**Nodules due to** *O. caecutiens* **and difficult to localize.**]—*Medicina.* Mexico. 1941. Sept. 25. Vol. 21. No. 396. pp. 409–413. With 9 figs. on 3 plates.

This paper from Mexico deals with the habitats of those Onchocerca worms that lie near the orbit and whose larvae enter the globe and produce blindness.

Nettel deals with three sets of habitats. 1. Periauricular nodules easily overlooked. 2. Nodules in muscles and attached to fascial planes. 3. Other deep nodules that remain undetected. Periauricular nodules may be superficial or deep. If they lie behind the auricle they may push it forwards away from the head, and one of the reproduced photographs shows this state present in one but not in the other ear; while removing a superficial nodule of this sort it is necessary to look deeper along the external meatus for yet larger ones, and in doing so as many as five have been found in a single ear. The seriousness of this condition is evident from the statement that of 40 blinded persons periauricular nodules were present in all, and they are apt to produce oedema of face and ear, the Onchocerca facies. The nodules on fascial planes, on tendons and in muscles are detected with difficulty, but as microphotographs show, adult females and microfilariae may lie among striped muscle fibres. The deeper nodules, even superperiosteal or subperiosteal, are unlikely to be detected clinically. They, even more than those located readily, constitute a grave threat to vision.

Clayton Lane.

MAUSS (Evelyn Abrams). **The Serum Fraction with which Anti-Trichinella** (*Trichinella spiralis*) **Antibody is associated.**—*Amer. Jl. Hyg.* 1941. Nov. Vol. 34. No. 3. Sect. D. pp. 73–80. [10 refs.]

"The albumin and globulin fractions of immune trichinous rabbit serum were subjected to 4 different tests for the presence of anti-trichinella antibody. The criteria used were complement fixation, circumlarval precipitate formation, reduced infectivity of larvae, and protective power for mice. The results obtained by the use of each of these methods demonstrated that the immunologically active fraction of trichinous rabbit serum was the fraction identifiable as

globulin. When the protein separation was effected by salt fractionation, the indication was that the antibody is more closely associated with the euglobulin than with the pseudoglobulin fraction."

DEFICIENCY DISEASES.

LEBLOND (C. P.) & CHAULIN-SERVINIERE (J.). **Spontaneous Beriberi of the Monkey as compared with Experimental Avitaminosis.**—*Amer. Jl. Med. Sci.* 1942. Jan. Vol. 203. No. 1. pp. 100–109. With 1 fig. [18 refs.]

Because so many of the symptoms and signs in human beriberi are not present in experimental vitamin B_1 deficiency in animals, the theory that thiamin deficiency is the sole cause of beriberi has been questioned. The appearance of spontaneous beriberi in a colony of monkeys (*Macacus sylvanus*) owing to the diet becoming partially deficient in thiamin provided an opportunity to investigate this point. Clinical signs of polyneuritis and cardiac failure, autopsy findings of peripheral nerve degeneration and hydropericardium were found in all the 20 monkeys studied. Adolescents were first affected, and in both these and the young, the disease was fatal; in adults the disease was more moderate and chronic. Thiamin therapy improved the condition but recovery from the polyneuritis was incomplete, suggesting that irreversible changes had occurred. When thiamin-free diets were given experimentally to two monkeys previously receiving the colony diet, death was rapid (33 and 40 days) and occurred before any prominent nervous or cardiac symptoms could appear. The only two adolescents that were not seriously ill were given this diet, developed acute symptoms and died within a few days. It is suggested that beriberi results only when there is partial thiamin deficiency. [This is not a new suggestion. It was brought forward by J. D. GRAHAM as long ago as 1927 (this *Bulletin*, 1928, Vol. 25, p. 433)].

H. N. Green.

MACHELLA (Thomas). **Studies of the B Vitamins in the Human Subject. III. The Response of Cheilosis to Vitamin Therapy.**—*Amer. Jl. Med. Sci.* 1942. Jan. Vol. 203. No. 1. pp. 114–120. [10 refs.] [Summary appears also in *Bulletin of Hygiene.*]

This paper summarizes the results of studies on 17 cases of cheilosis. Fifteen of these showed other signs of deficiencies in the vitamin B complex, 16 had anorexia and in three there was clinical and laboratory evidence of scurvy. The cheilosis varied in its response to treatment with different vitamins: 9 of 13 cases responded to pyridoxine, 2 of 3 to nicotinic acid, 2 (after unsuccessful treatment with riboflavin and pyridoxine) to brewers' yeast, 3 (cases of scurvy) to ascorbic acid. Eight of these patients had received riboflavin without success. Cheilosis, which is usually attributed to riboflavin deficiency, has been shown by other workers to respond to the administration of other vitamins in B-complex. Whether the lesion can be caused wholly or in part by a deficiency of different vitamins, or whether the treatment of one deficiency state, by restoring the appetite, brings about an increased intake of some substance which causes healing, is not clear.

H. N. Green.

PAWEL (Martinus). A vitamina PP. I–XVII. [**The PP Factor of Vitamin B.**]—Reprinted from *Rev. Gastro-Enterologia São Paulo.* 1940. Aug., Oct. & Dec. 1941. Feb. Vol. 3. Nos. 3, 4, 5 & 6. pp. 85–101 ; 115–126 ; 145–160 ; 183–218. [365 refs.]

To abstract this monograph or series of papers on the PP factor is impossible. The whole is a highly condensed and amply documented statement of the various aspects of this much debated subject. The author discusses the pellagra-preventing activity of certain of the pyridin compounds and the biological specificity of the factor, its metabolism, the bio-chemistry of glycolysis, the possible connexion with porphyrin excretion and the effect of sulphur. STANNUS's articles in this *Bulletin* in 1936 and 1937 on Pellagra and Pellagra-like conditions are referred to, and the author acknowledges his indebtedness to this writer by dedicating the present work in the following pleasing terms : " Offer to the great studious on pellagra, Prof. H. S. Stannus, from the Author." Readers of this *Bulletin* will be glad to see this acknowledgment of one who has for years interested himself in this field of work.

H. H. S.

GIRI (K. V.). **The Anti-Pellagra Factor.**—*Indian Med. Gaz.* 1942. Feb. Vol. 77. No. 2. pp. 98–107. [105 refs.]

VILTER (Richard W.), BEAN (William B.) & SPIES (Tom D.). **The Effect of Yeast and Muscle Adenylic Acid in Malnourished Persons with Pellagra and Peripheral Neuritis.**—*Jl. Lab. & Clin. Med.* 1942. Jan. Vol. 27. No. 4. pp. 527–530.

Among the many compounds present in yeast and crude liver extracts is adenylic acid which, like thiamin, riboflavin, and nicotinic acid, is a component of a number of organic catalysts essential for cell respiration, including coenzymes I and II, xanthine oxidase, d-amino acid oxidase and the yellow enzyme.

The effect of the administration of adenylic acid prepared either from yeast or from muscle was studied in some small groups of cases.

Group I. Sixteen patients who had had pellagra in the past, been cured and then relapsed, in that six exhibited ulcerative lesions on the tongue, and 10 non-ulcerative glossitis and burning sensations in the mouth. Two of the 10 patients also showed signs of ariboflavinosis—conjunctivitis, circum-corneal injection and cheilosis. There was rapid response of these mouth symptoms to intravenous injection of 50 mgm. adenylic acid (14 muscle and 2 yeast preparations) dissolved in saline ; the injections were given twice daily for one to three days.

Group II. Four patients suffering from weakness, insomnia, irritability, etc.—symptoms of the pre-pellagra state. Similar satisfactory response was obtained.

Group III. Six patients (five alcoholics and one pellagrin) suffering with symptoms of peripheral neuritis refractory to treatment with thiamin and brewer's yeast. In response to the administration of 25 mgm. twice daily, within 21 days spontaneous pain and hyperaesthesia disappeared, perception of touch and vibration sense returned, and they were able to walk.

Group IV (which served as a control to I and II). Three patients suffering from recurrent superficial ulceration of the tongue but whose diet was considered adequate. There was no response to adenylic acid or to nicotinic acid.

The authors advise against adenylic acid for general therapeutic use as severe reactions are common, including flushing of the face, hyperpnoea, tachycardia with electrocardiographic changes, abdominal cramps, apprehension and a sense of impending disaster. Note is made that the exhibition of adenine sulphate has no apparent effect.

H. S. Stannus.

MISCELLANEOUS.

PANAMA CANAL. **Report of the Health Department of the Panama Canal for Year 1940** [STAYER (M. C.), Chief Health Officer.]—pp. vi+122.

v. LUTTEROTTI (M.). Beobachtungen ueber Ulcus tropicum in Italienisch-Ostafrika. [**Observations on Tropical Ulcer in Abyssinia.**]—*Deut. Trop. Ztschr.* 1941. Dec. 1. Vol. 45. No. 23. pp. 697–712. With 5 figs. [20 refs.]

The author classifies tropical ulcer into :—(1) the primary phagedaenic type, (2) the non-phagedaenic type, and (3) the secondary phagedaenic type. The primary phagedaenic ulcer may be of the kind which penetrates deeply through the tissues, and this is the common form, or it may fail to pass beneath the superficial fascia, but may spread widely. These ulcers commonly commence in abrasions or small wounds, and are most often seen on the lower part of the leg. Non-phagedaenic ulcers are not so common ; they may be superficial or may spread deeply, they are usually very chronic and show little tendency to heal. These ulcers may arise from phagedaenic forms through the disappearance of purulent discharge and false membrane ; they present a granulating surface, but epithelialization is extremely slow. Secondary phagedaenic processes may arise in tropical ulcers which have lost their primary phagedaenic character, and have become torpid.

Of 82 cases seen by the author there was in 70 a history of trauma which provided the starting point ; in the other 12 it is possible that some slight injury occurred but was overlooked. Although trauma is so frequently associated with the onset, however, other factors undoubtedly influence the development and nature of the ulcers, and of these factors the state of nutrition, the general health, the climate and, to some extent, the race of the patients, are important. The patients seen by the author were chiefly native soldiers, and were of three tribes : Amharas, who live at altitudes of 2,000 to 2,500 metres, Gallas from similar heights, and Sudanese from the region of Kassala. The Gallas appeared to be most susceptible and to show least tendency towards healing ; the Amharas were least affected. Living conditions were good and were the same for all, and the soldiers were all young and healthy.

In the civil population tropical ulcer is rare in the highlands, and is rarer in the cool, damp season of the year than in the hot and dry season. More severe forms are seen in the general population than in the soldiers, especially among the Shenasha tribe, who are badly nourished and in whom malaria is endemic. The author considers that yaws and syphilis play little part in the aetiology of the disease.

In treatment, good results have been obtained with a dressing of 10 per cent. zinc oxide ointment, 10 per cent. ichthyol ointment and Metchnikoff's calomel ointment, in the proportions 3 : 2 : 1, to which are added 5 per cent. xeroform and 2 per cent. iodoform. The ulcer should first be cleaned with a sharp spoon under Evipan narcosis. For chronic ulcers elastic strapping is useful. Prophylaxis consists of immediate attention even to trivial wounds of the legs. *C. W.*

BLANC (Georges) & BALTAZARD (Marcel). Transmission du bacille de Whitmore par la puce du rat " Xenopsylla cheopis." [**Transmission of *Pf. whitmorei* by *X. cheopis*.**]—*Presse Méd.* 1941. Dec. 3–6. Vol. 49. Nos. 104–105. p. 1293.

The following is a translation of a short account of a paper read at the Académie des Sciences, Paris, on October 20th, 1941 :—

" The fact that infection with *Pf. whitmorei* is common to rodents and man raises the question of transmission by biting insects.

" The first results of experiments made with rat fleas seem to justify this hypothesis. The bacillus develops in *Xenopsylla cheopis* in a manner similar to that of the plague bacillus. It multiples within the body of the insect, is maintained alive for 50 days at least, and can be transmitted by bite or in the faeces.

" It therefore seems possible to state that in nature infection with *Pf. whitmorei* can be transmitted from rodent to rodent, if not from rodent to man, by the flea."

[In a later communication (*Presse Méd.*, 1942, Jan. 7–10, p. 33, and *C. R. Acad. Sci.*, 1941, Vol. 213, pp. 670–672) the authors show that *Aëdes aegypti* can become infected and can transmit by bite. They conclude that many arthropods can transmit, that there is no specificity, and that arthropod transmission (if it occurs) may depend on the habits of the arthropods, those which pass most freely from rodents to man having the best chance of transmission.] *C. W.*

VINTON (K. W.) & STICKLER (W. H.). **The Carnero, a Fish Parasite of Man and Possibly of Other Mammals.**—*Amer. Jl. Surgery.* 1941. Nov. Vol. 54. No. 2. pp. 511–519. With 7 figs.

The carnero or candirú is a small member of the catfish family Pygidiidae. It is long and slender, 5–6 inches long, and a little less than a lead pencil in diameter. It is of the genus Vandellia and has a ventrally placed mouth with 5 teeth in the upper jaw and spines on the lower parts of each operculum. They are commonly ectoparasitic on Siluroid fish, living in their gills, where the teeth and spines start a flow of blood which is sucked up by the parasite. They bore into the urethra of persons when bathing and cause copious and severe bleeding. Animals may be similarly attacked. The species known to attack man is *V. plaizae*. The head and spines would seem to be under muscular control so that the fish can withdraw if it wills.

The treatment seems to be quite effectual, a preparation of the unripe fruit of the *jagua* tree, *Genipa americana*. " The centres of the smaller green fruits are scraped out, mashed and squeezed and mixed with water, the strength of the preparation varying considerably . . . . It

is taken by mouth." The patients may be nauseated but in a short time, from a few minutes up to 2 hours, the fish is dislodged. This remedy has been used by the natives for generations.

Several questions remain to be studied, which the author mentions, among them the following: 1. How does the fish obtain oxygen while in the host's body? 2. How long can it live as an internal parasite? 3. Will it eventually leave the host of its own accord? 4. Is it really a blood-feeder or are the injuries purely mechanical? 5. If the former, what does it feed upon when it cannot find blood? [But, if it normally lives in the gills of Siluroid fishes, there would be no time when it could not find blood.] 6. How does the *jagua* juice bring about dislodgement? *H. H. S.*

SYMES (C. B.), MCMAHON (J.) & HADDOW (A. J.). **Pyrethrum Powder: a Preliminary Note on its Use in the Control of Insect Vectors of Diseases.**—*East African Med. Jl.* 1942. Mar. Vol. 18. No. 12. pp. 360–376.

This paper contains a preliminary account of the effects of dusting with pyrethrum powder, usually the standard fine or second grade, on insect pests in houses in Kenya. When experimental huts measuring 11 feet in diameter and 7 feet high to the cloth ceiling were dusted at sundown with 1–2 oz. of the powder, no living mosquitoes were found during the next 12 hours or so. The mosquito populations in the treated huts remained from 42–68 per cent. below those in the control huts during the next three days, and there was still an appreciable effect at the end of 30 days. Light dusting with pyrethrum powder in the houses of Africans in Nairobi also destroyed large numbers of cockroaches, bed-bugs, house flies, beetles, etc. Experiments in the laboratory have demonstrated its efficiency against fleas and lice. A further use has been to check fly breeding in pit latrines. The rather heavy dose of 3 oz. of second grade powder per seat per week has proved successful in controlling well established fly breeding in 4 weeks. The authors advocate the extended use of the powder (*a*) for the reduction of vermin in native quarters, barracks, etc.; (*b*) against loose fleas and lice in and around quarters; (*c*) as an antimalarial measure against mosquitoes in quarters of all kinds; (*d*) for the control of house fly breeding. No instances of any type of reaction to the powder have occurred among the thousands of Africans whose quarters have been treated. *V. B. Wigglesworth.*

MACPHERSON (Ronald K.). **Harara among Australian Soldiers.** [Correspondence.]—*Med. Jl. Australia.* 1941. Oct. 25. 28th Year. Vol. 2. No. 17. p. 493.

Harara is described by THEODOR as an allergic reaction to the bites of Phlebotomus at the height of sensitization [see this *Bulletin*, 1936, Vol. 33, p. 445]. Men of the Australian Forces have suffered severely in northern Palestine. Exposed skin becomes covered with hard weals up to one centimetre in diameter; these may subside or may be replaced by blisters which may later become infected, and in some cases the regional lymph glands may be enlarged and tender. *C. W.*

STRICKLAND (C.) & ROY (D. N.). **Myiasis-producing Diptera in Man.**—*Indian Jl. Med. Res.* 1941. Oct. Vol. 29. No. 4. pp. 863–865.

Identification was made of 36 specimens from cases of human myiasis, between 1922 and 1941 ; the following flies were recognized :—*Chrysomyia bezziana*, Sarcophaga spp., Drosophila sp. and *Apiochaeta scalaris*. Most of the cases were of intestinal myiasis, but nasal, ocular, aural, dental and cutaneous cases were reported. One of these flies only, *C. bezziana*, is biontophagous ; as a rule the patients complained of few symptoms, but in one case the larva of *C. bezziana* was found within the dura mater of the spinal cord. *C. W.*

DES LIGNERIS (M. J. A.). **The Production of Benign and Malignant Skin Tumours in Mice Painted with Bantu Liver Extracts.**—Reprinted from *Amer. Jl. Cancer.* 1940. Aug. Vol. 39. No. 4. pp. 489–495. With 5 figs.

Although the different races of man appear to be about equally subject to cancer, there are pronounced variations in the local incidence of the disease among them. An example of this is the high frequency of hepatic cancer among the Malays and the Bantus of Africa. It occurred to Des Ligneris that an examination of liver extracts from Bantus, with or without cancer, and from Europeans, might throw light on the matter. He prepared extracts and applied them to the skin of mice in the interscapular region according to the usual method for testing carcinogenic potency. In the first experiment 100 mice were painted with an extract of liver dissolved in petroleum ether ; 21 of the mice survived for 8 months and of these eight had papillomata at the site of application, two of the lesions being cancerous. In a second experiment 300 mice were divided into three groups of 100. The mice of group I were painted with an extract of noncancerous European liver, group II with a preparation from noncancerous Bantu liver, and group III with an extract of cancerous Bantu liver. The results, recorded eight months later, may be tabulated as follows :—

Group	No. of Survivors	No. with Papillomata	No. in which Papillomata were malignant
I	72	0	0
II	73	5	2
III	71	7	3

Experiments with oestrogens have already proved that carcinogens may be of endogenous origin ; the experiments of Des Ligneris open a wider aspect of this problem.

Others have tested extracts of liver on lines somewhat like those of Des Ligneris and have attained comparable results. Among these investigators are KLEINENBERG, NEUFACH & SHABAD [*Amer. Jl. Cancer*, 1940, Vol. 39, p. 463] and HIEGER [*ibid.*, 1940, Vol. 39, p. 496]. Hieger obtained sarcomas in 12 among 367 mice at the site of injection of liver extracts. *Harold Burrows.*

CORDIER (Daniel). Physiologie des climats désertiques et tropicaux. Lutte contre la chaleur. [**Physiology of Desert and Tropical Climates. Heat Regulation.**]—36 pp. With 7 charts. London: Editions de la France Libre Ltd., 4 Carlton Gardens, S.W.1.

The extension of fighting in the present war to most quarters of the world has placed a great additional burden on those responsible for the health and well-being of the troops. Now that operations are proceeding in all continents and under all latitudes, a knowledge of body-heat regulation under conditions varying so widely in their physiological effects is essential. As a justification for this point of view the author, in an introductory section, quotes statistics for the war of 1914–1918. In a series of colonial expeditions the numbers of military effectives who died from maladies and other climatic effects were more than double of those who were killed in action or who died later of their wounds.*

The handbook deals with much of the work that has been carried out in recent years by various workers on the effects of environment on the human organism. The physiological characteristics of desert and tropical climates are reviewed. The circulatory variations necessary for thermoregulation under such conditions are discussed, together with the effects of environment on perspiration, both sensible and insensible. The salt and water losses caused by sweating are described and the necessity for the maintenance of salt balance under the influence of high temperatures is stressed. The effect of acclimatization in modifying the sweat secretion is illustrated by the results of different workers.

In conclusion, some of the physio-pathological troubles caused by heat, *viz.*, heat stroke, exhaustion, sunstroke and heat cramps, are discussed. The author has performed a useful service by compressing much information into a small compass. *C. G. Warner.*

* This has been noted in all campaigns. The following figures (the nearest integer per thousand strength) are taken from SCOTT's *History of Tropical Medicine*, quoting NOTTER & FIRTH :—

Campaign.	Admissions.		Deaths.	
	Disease.	Wounds.	Disease.	Wounds.
Ashanti, 1873–4	474	70	16	6
Zululand, 1879–80	739	12	25	2
Afghanistan, 1879–80	870	51	36	7
Egypt, 1882	554	29	6	7
Sudan, 1885–6	1,100	47	29	10
Ashanti, 1895–6	49	—	0·5	—
Chitral, 1895	1,530	14	49	5
Nile, 1898	1,101	57	36	16
South Africa, 1899–1901 ...	746	34	69	42

SPECIAL RESEARCH SECTION.*

MURRAY (A. J.) & CROCKET (J. A.). **Interim Report on the Prevalence of Silicosis and Tuberculosis among Mine Workers in the Gold Coast.** 17 pp. 1941. Accra, Gold Coast Colony. [1*s.*] [Summary appears also in *Bulletin of Hygiene.*]

The gold mines in the Tarkwa area were the site of this investigation, which took place in 1940. Gold mining in the Gold Coast began near the end of the 19th century, increased up to the last war, after which there was a depression. Revival commenced in 1934, since when the mining population and the output have expanded rapidly; in 1939 the total labour employed by the 22 gold mining companies was 900 Europeans and 30,500 Africans; somewhat less than one-half of these worked underground. In each mining district, only a small proportion of the native labour is derived locally. The native usually works for one or two years in the mines and then goes home; he may return to the mines for one or two more similar periods. For the majority of native workers, mining is thus migratory and intermittent, though a minority stay in the mining area and remain continuously in the industry. Out of 13,000 underground employees in eight of the larger mines, only 6 per cent. had had more than five years' service with the same company. While at the mines the native employees live in nearby villages with their families, in contrast to the compound system in South Africa.

The ore mined in the Gold Coast consists of a quartz gold-bearing reef and a banket conglomerate formation, the latter being worked in the Tarkwa area under investigation. The free silica in the ore varies from about 65 per cent. to about 80 per cent., but the samples are clearly insufficient for any but a rough estimate.

The investigation included: (i) tuberculin testing of 800 underground employees; (ii) radiographical and physical examination of 560 native underground employees from various mines in the Tarkwa area, with a bias towards longer-service men; over half had seen more than five years' underground service with the company concerned, but only about one-fifth had seen more than 10 years of such service; (iii) post mortem examination of 20 ex-miners. The results of the tuberculin tests are not presented in this report. The X-rays were classed as (*a*) (1) no abnormality detected, and (2) slight increase in linear striation; (*b*) gross increase in linear striation; (*c*) silicosis (including silico-tuberculosis where the tuberculosis was latent or inactive); (*d*) silicosis with active tuberculosis; (*e*) active tuberculosis (including those where silicosis was a possible but not certain accompaniment); (*f*) doubtful; and (*g*) other pulmonary diseases.

Of the 560 men examined, 21 had definite silicosis (on a high standard of diagnosis), 10 without and 11 with accompanying active tuberculosis. In the former group, three were early, four moderately advanced and three advanced. All the cases were in men with more than four years' underground service. In addition to the 21 cases classed as silicosis there were 39 showing gross increase in linear striation.

Further than that the predisposing occupations for silicosis were those of machine boy, hammer boy and blast boy, little comment

* It is hoped to place reviews of interim reports of uncompleted work in this section from time to time.

could be made upon the working environment ; it is stated that with free use of water underground the humidity of certain working places must approach close to saturation. No dust counts were available.

Owing to the inclusion of a number of cases of known tuberculosis among the 560 underground miners, the prevalence of the latter disease was estimated from 380 who were unselected in this respect ; in this group were 4 cases of active pulmonary tuberculosis with silicosis and 20 cases without definite silicosis, making a total tuberculosis incidence of 6 per cent. ; in addition to these definite cases, some of those showing increased linear striation may have been tuberculous.

The incidence of pulmonary tuberculosis was, from these figures, higher than that of silicosis, and the authors regard tuberculosis as the greater menace to the health of mine employees. The majority of the cases of tuberculosis found were entirely unsuspected by the mine medical authorities and none appeared to be receiving medical attention. Comparisons with the surrounding non-mining population were not available but indirect evidence suggested that the high incidence among these miners was related to the nature and conditions of their employment.

The post mortem examinations of 20 former underground workers showed typical silicotic nodulation in 6 from naked-eye appearances, and in another 7 from microscopical examination. In all but two cases the cause of death was pulmonary tuberculosis.

This interim report clearly shows a significant prevalence of silicosis and tuberculosis in these Gold Coast mines. Owing to the recent rapid expansion, there is at present a disproportionately large number of men of short service, but, if the output is to be maintained, there will in the future be a relative increase in long-service employees ; since the incidence of silicosis and tuberculosis increases with the length of employment, this will mean an increase of these diseases, other things being equal. In the authors' opinion, further investigation is needed, and to aid this they suggest (*a*) that compulsory registration of all mine labour be introduced, such registration to include complete and reliable particulars of the industrial history ; (*b*) that in order to obtain an approximation of the incidence of pulmonary tuberculosis in various parts of the colony this disease be made notifiable ; (*c*) that it is highly desirable that complete records of dust counts and underground atmospheric conditions be kept and be available.

[The fact is already evident from this interim report that silicosis is an industrial hazard in gold mines in the Gold Coast. While prevention of the disease must be the ultimate objective, the immediate measures called for include early diagnosis and a compensation scheme (which apparently does not exist). As is the case with gold mining in South Africa and as is being increasingly advocated in coal mining in the U.S.A., it will be well to include tuberculosis in any scheme of compensation that is primarily designed for silicosis. At present little or nothing appears to be done for native miners in the Gold Coast who suffer from either of these diseases. In the present report it is stated that when a native feels himself seriously ill he usually tries to return to his own country, a step not usually discouraged by the Mine Medical Officer as it removes an unfit and infectious person from the camp ; former mining employees with the disease who are unable to make the journey home are frequently entered in the Register of Deaths at Tarkwa as "beggars." The suggestion that tuberculosis be made notifiable throughout the Colony is not likely to be very helpful. Even

in Great Britain notification is defective, and to form an estimate of prevalence on the basis of notifications in the Gold Coast, which must inevitably be grossly incomplete, would lead to the formation of a seriously misleading picture. Comparison between miners and general population is only valid if samples of the population are examined as fully as the groups of miners. Extension of post mortem examinations and of sputum examination in all cases of chronic cough should be undertaken. Pre-employment X-ray examination for miners would be valuable. It may be advisable also to test recruits with tuberculin, and to exclude from mine labour those who react strongly. In South Africa these strong reactors have been found particularly liable to break down with tuberculosis after a period of labour.]

P. D'Arcy Hart.

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